

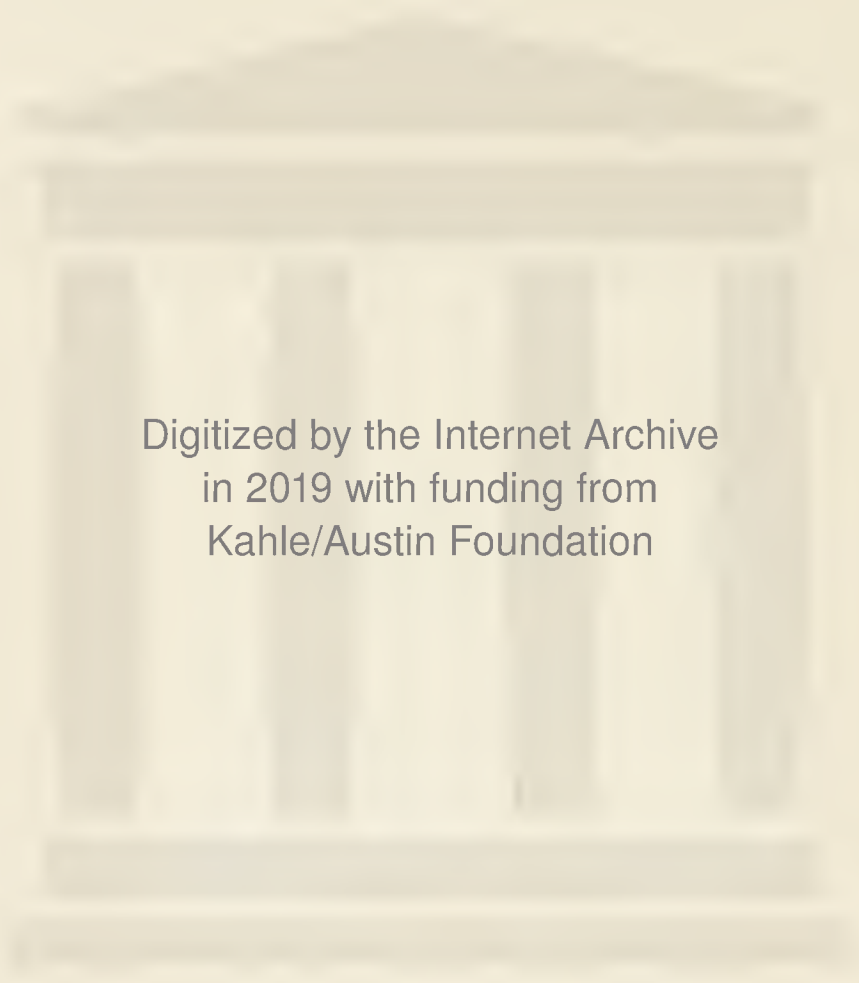
ORGANIC SYNTHESES

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ORGANIC SYNTHESSES

AN ANNUAL PUBLICATION OF SATISFACTORY
METHODS FOR THE PREPARATION
OF ORGANIC CHEMICALS

VOLUME 41

1961

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NOMENCLATURE

Preparations appear in the alphabetical order of common names of the compounds. For convenience in surveying the literature concerning any preparation through *Chemical Abstracts* subject indexes, the *Chemical Abstracts* indexing name for each compound is given as a subtitle if it differs from the common name used as the title.

SUBMISSION OF PREPARATIONS

Chemists are invited to submit for publication in *Organic Syntheses* procedures for the preparation of compounds which are of general interest, as well as procedures which illustrate synthetic methods of general utility. It is fundamental to the usefulness of *Organic Syntheses* that submitted procedures represent optimum conditions, and the procedures should have been checked carefully by the submitters, not only for yield and physical properties of the products but also for any hazards that may be involved. Full details of all manipulations should be described, and the **range** of yields should be reported rather than the maximum yield obtainable by an operator who has had considerable experience with the preparation. For each solid product the melting-point **range** should be reported, and for each liquid product the **range** of boiling point and refractive index should be included. In some instances, it is desirable to include additional physical properties of the product, such as ultraviolet, infrared, or nuclear magnetic resonance spectra. The methods of preparation or sources of the reactants should be described in notes, and the physical properties (such as boiling point, index of refraction, melting point) of the reactants should be included except where rather standard commercial grades are specified.

Procedures should be written in the style and format employed in the latest published volume of *Organic Syntheses*. Copies of

the current style sheet may be obtained from the Secretary of the Editorial Board. In section 3, **Methods of Preparation**, there should be described other practical methods for preparing the compound which have appeared in the literature. It is unnecessary to mention methods which have been published but are of no practical synthetic value. There should also be included a statement of the merits of the preparation which recommend it for publication in *Organic Syntheses* (synthetic method of considerable scope, specific compound of interest, method gives better yield or is less laborious than other methods, etc.). This information is necessary because subsequent volumes of *Organic Syntheses* will include under **Merits of Preparation** a statement explaining why the preparation is published in *Organic Syntheses*. Two copies of each procedure should be submitted to the Secretary of the Editorial Board. It is sometimes helpful to the Board if there is an accompanying letter setting forth the features of the preparation which are of interest.

Additions, corrections, and improvements to the preparations previously published are welcomed and should be directed to the Secretary.

EDITOR'S PREFACE

Organic Syntheses was founded under the leadership of Roger Adams at the end of World War I for the purpose of providing tested procedures for preparing useful organic compounds in reasonable quantities. The need was urgent because supplies of organic chemicals from abroad were then no longer available.

Since the founding of *Organic Syntheses*, the requirements for starting materials for research in organic chemistry have steadily changed. Today there are commercial sources for an almost incredible variety of organic compounds. Furthermore, with the advent of new methods for separation, identification, and analysis, reactions are being studied with ever-decreasing quantities of starting materials. Although its basic format has remained unchanged, *Organic Syntheses* has moved to meet the needs of current research. Emphasis is now strong on providing examples of new and general types of reactions and compounds. More than a third of the reactions and compounds described in this volume were unknown five years ago. Indeed, for the extraordinary conversion of carboxylic acids to trifluoromethyl groups by sulfur tetrafluoride (p. 104), an illustrative procedure is offered within eighteen months of the time of the original publication.

Among the features of Volume 41 is the smallest-scale synthesis yet published in *Organic Syntheses*, namely, the preparation of 0.0005 mole of cholestanyl methyl ether by a generally useful methylation procedure that employs diazomethane and fluoboric acid (p. 9). Two preparations of isocyanides by dehydration of formamides are included. One of these, illustrated by cyclohexyl isocyanide (p. 13), is most suitable for aliphatic isocyanides; while the other, illustrated by *o*-tolyl isocyanide (p. 101), is most suitable for aromatic isocyanides.

Current interest in cyclopropanes is reflected by two preparations: Norcarane from cyclohexene, methylene iodide, and zinc-copper couple (p. 72) illustrates a new way of adding a methylene

group to an olefin; the addition of dichlorocarbene to dihydropyran (p. 76) involves generation of the carbene from ethyl trichloroacetate and sodium methoxide. Two Kolbe electrolytic syntheses are described. Dimethyl 1,18-octadecanedioate (p. 33) from methyl hydrogen sebacate presents nearly optimum conditions for Kolbe electrolyses, while 2,7-dimethyl-2,7-dinitroöctane (p. 24) from 4-methyl-4-nitrovaleric acid illustrates the use of a separate anode compartment to minimize reduction of sensitive functional groups, here the nitro group.

Phenacylamine hydrochloride (p. 82) affords a thoroughly documented and general procedure for conversion of $\text{—CHNH}_2\text{—CH}_2\text{—}$ to $\text{—COCH(NH}_2\text{)—}$ by way of methoxyethylenimine intermediates. Preparation of allyllithium by cleavage of allyltriphenyltin with phenyllithium is illustrated by 4,6-dimethyl-1-hepten-4-ol (p. 30). The procedure for synthesizing allyllithium can also be adapted to the preparation of benzyllithium and vinylolithium. Use of 1,4-addition of Grignard reagents to *sec*-butyl esters of α,β -unsaturated acids as a means of synthesizing aliphatic acids is illustrated by 3-methylheptanoic acid (p. 60).

A hitherto unpublished preparation of diazomethane is given on p. 16. The starting material is the commercially available bis-(*N*-methyl-*N*-nitroso)-terephthalamide, and the procedure conveniently affords 0.76 to 0.86 mole of ethereal diazomethane. Ozonization in polar solvents is illustrated by two preparations (pp. 41 and 46). Many other unusual and interesting preparations are included, such as ruthenocene (p. 96), *N,N*-diethyltrichlorovinylamine (p. 21), phenyl *tert*-butyl ether (p. 91), and tetramethylammonium 1,1,2,3,3-pentacyanopropenide (p. 99).

Inclusion of many preparations of current interest has been possible only as the result of an active solicitation program. The Editorial Board welcomes suggestions for solicitations of examples of new and generally interesting types of reactions and compounds.

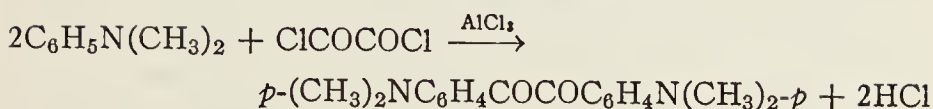
JOHN D. ROBERTS

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4,4'-BIS(DIMETHYLAMINO)BENZIL

[Benzil, 4,4'-bis(dimethylamino)-]



Submitted by CELAL TÜZÜN, MICHAEL OGILARUSO, AND
ERNEST I. BECKER.¹

Checked by B. C. MCKUSICK and R. J. SHOZDA.

1. Procedure

In a 3-l. three-necked flask equipped with an efficient mechanical stirrer of high torque (Note 1), a reflux condenser with a calcium chloride drying tube, a thermometer, and a dropping funnel are placed 133 g. (1.00 mole) of anhydrous aluminum chloride and 200 ml. of dry carbon disulfide. The mixture is cooled in an ice bath and stirred while 182 g. (1.50 moles) of N,N-dimethylaniline (Note 2) is added through the dropping funnel during a period of 15 minutes. The dropping funnel is rinsed with 20 ml. of carbon disulfide which is then run into the flask. Any aluminum chloride sticking to the walls of the flask is now scraped into the mixture, which is an easily stirred slurry of a white solid in a light-green liquid.

The reaction mixture is cooled to 5–10° in an ice-salt bath (Note 3), and, with continued stirring, a solution of 31.7 g. (21.3 ml., 0.250 mole) of oxalyl chloride in 200 ml. of dry carbon disulfide is added through the dropping funnel in the course of 20 minutes. After the addition is complete, the thick black reaction mixture is allowed to warm to room temperature, refluxed for 1 hour, and then cooled to 0–5° in an ice bath. The mixture is stirred throughout these steps. One hundred grams of chipped ice is added with stirring, followed by 400 ml. of cold water. Steam is then passed into the flask until the carbon disulfide and unreacted dimethylaniline are removed, and the green-black

aluminum complex is decomposed to a mixture of a green solid and a blue solid; this requires 1–2 hours (Note 4). The mixture is cooled to 50°, and the solid, which is principally 4,4'-bis(dimethylamino)benzil, is collected on a Büchner funnel. In order to remove the major part of the impurity, which is somewhat soluble in water, the solid is slurried in 200 ml. of water at 50°, and the slurry is filtered. This process is repeated twice, and the crude benzil, now a green solid, is washed successively on the funnel with 200 ml. of water at 50° and with 100 ml. of cold methanol. After being dried in air, it weighs 44–55 g. and melts at 191–196°.

The crude benzil is dissolved in 500 ml. of chloroform. To remove the impurity that remains (Note 5), the solution is shaken with three 400-ml. portions of 6% aqueous hydrogen peroxide solution containing 1.0 g. of sodium hydroxide in each portion, and finally with 500 ml. of water. The aqueous layers are combined, warmed to drive off dissolved chloroform, and filtered to separate about 1.5 g. of a yellow-green solid, which is dissolved in the chloroform solution.

The chloroform layer is distilled to dryness and the residue is dissolved in 1.5 l. of acetone under reflux. The hot acetone solution is filtered and then allowed to cool in a refrigerator. Yellow 4,4'-bis(dimethylamino)benzil crystallizes from the acetone solution. It is separated by filtration and washed with 100 ml. of cold methanol. After being dried in air, it weighs 28–31 g. (38–42%); m.p. 200–202°; $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$ 371 m μ (ϵ 44,700) (Note 6).

The acetone filtrate is concentrated to 700 ml. and cooled to 0–5°. An additional 4–8 g. (6–11%) of slightly less pure benzil, m.p. 198–201°, crystallizes from solution (Note 7).

2. Notes

1. A magnetic stirrer is unsatisfactory. The submitters used a glass-blade stirrer at 300 r.p.m. The stirrer shaft must be rigidly attached to the motor because the reaction mixture becomes very thick during the addition of oxalyl chloride.

2. Eastman Kodak white label compounds used without further purification are satisfactory starting materials.

3. Cooling below -10° should be avoided because the reaction stops at that temperature and large amounts of oxalyl chloride accumulate in the flask. If this mixture is then allowed to come to room temperature, a vigorous reaction that may get out of control will take place. It is probable that, at reaction temperatures about 10° , the yield of 4,4'-bis(dimethylamino)benzil is less and some Crystal Violet is formed as an impurity, for it has been reported that aluminum chloride effects the conversion of N,N-dimethylaniline and oxalyl chloride to Crystal Violet in 92–95% yield when the reaction is allowed to proceed without cooling.²

4. The submitters recommend that the following purification procedure be used from this point for the preparation of 4,4'-bis(diethylamino)benzil (72% yield) and 4,4'-bis(di-*n*-propylamino)benzil (58% yield). The procedure has also been used as an alternative to the one given for 4,4'-bis(dimethylamino)benzil.

One liter of water is added, making the total volume about 2 l., and, after the solution has been cooled to room temperature, it is extracted with 1 l. of chloroform and then with 150 ml. of chloroform. The combined dark-blue extracts are washed with 550 ml. of 8.5% hydrochloric acid, then with 200 ml. of water and dried over anhydrous sodium sulfate. The chloroform solution is distilled until the volume is 250 ml., and it is then passed through an 8.5 x 25-cm. column (300 g.) of Alcoa F-20 alumina. The adsorbate is eluted with 1 l. of chloroform. The eluate is evaporated to a volume of 250 ml., washed with 500 ml. of 10% sodium hydroxide solution then with 100 ml. of water, and distilled to essential dryness.

The residual crude, yellow, semi-solid product is stirred and brought to a boil with 250 ml. of ethyl acetate and then allowed to cool to room temperature while stirring. Filtration affords 39–41 g. (52–55%) 4,4'-bis(dimethylamino)benzil, m.p. $201-203^{\circ}$. Concentration of the mother liquor to 50 ml. gives, after cooling, an additional 3.5–4.5 g. of product, m.p. $175-180^{\circ}$. Recrystallization of 10 g. of the combined products from 120–150 ml. of benzene gives 9.1–9.3 g. of yellow crystals, m.p. $202-203^{\circ}$.

5. The checkers found that at least part of the colored impurity is Crystal Violet. Alkaline hydrogen peroxide is reported to

cleave Crystal Violet to N,N-dimethylaniline and Michler's ketone.³

6. The product is sometimes pale green because of traces of impurities, but it is nevertheless very pure, for repeated recrystallization does not change ϵ_{\max} .

7. Addition of 1 l. of cold water to the acetone filtrate from which the second crop of benzil is separated causes about 5 g. of impure benzil to precipitate. This may be added to the crude benzil of a subsequent run prior to the treatment with hydrogen peroxide and alkali.

3. Methods and Merits of Preparation

4,4'-Bis(dimethylamino)benzil has been made previously by heating a mixture of oxalyl chloride and N,N-dimethylaniline under a pressure of 300 atmospheres of carbon monoxide in a steel pressure vessel at 100°. ⁴ The present method is simpler and gives better yields. As 4-dimethylaminobenzaldehyde cannot be converted to the corresponding benzoin,⁵ this common route to benzils cannot be used to prepare 4,4'-bis(dimethylamino)benzil.

The present procedure is reported by the submitters to be a general way of making 4,4'-bis(dialkylamino)benzils and, with a somewhat modified purification scheme (Note 4), has been used by them to prepare 4,4'-bis(diethylamino)benzil from N,N-diethylaniline and 4,4'-bis(dipropylamino)benzil from N,N-dipropylaniline.

¹ Polytechnic Institute of Brooklyn, Brooklyn 1, N. Y.

² G. v. Georgievics, *Ber.*, **38**, 884 (1905).

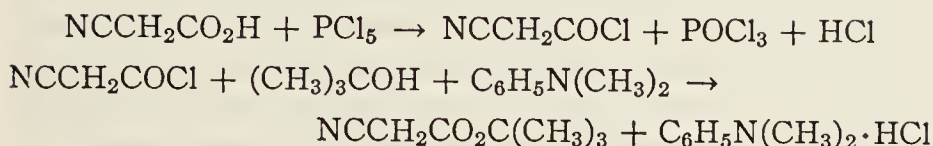
³ I. N. Postovskii, *J. Chem. Ind. (U.S.S.R.)*, **4**, 552 (1927) [*C.A.*, **22**, 957 (1928)].

⁴ H. Staudinger and H. Stockmann, *Ber.*, **42**, 3485 (1909).

⁵ S. M. McElvain, "The Acyloins," *Org. Reactions*, **4**, 273 (1948).

tert-BUTYL CYANOACETATE

(Cyanoacetic acid, *tert*-butyl ester)



Submitted by ROBERT E. IRELAND and MICHAEL CHAYKOVSKY.¹

Checked by MAX TISHLER and ARTHUR J. ZAMBITO.

1. Procedure

In a 5-l., three-necked, round-bottomed flask equipped with a rubber- or mercury-sealed mechanical stirrer and a reflux condenser carrying a drying tube are placed 340 g. (4 moles) of cyanoacetic acid (Note 1) and 2 l. of anhydrous ether. To the stirred solution, 834 g. (4 moles) of phosphorus pentachloride is added in portions through the third neck of the flask, which is sealed between additions. The mixture is cooled occasionally with an ice bath to prevent excessive refluxing, and, after the addition is complete, stirring is continued for 0.5 hour or until the phosphorus pentachloride dissolves completely. The reflux condenser is removed and replaced with apparatus for downward distillation (Note 2), and the ether is distilled from a water bath at 50–60° (Note 3), after which most of the phosphorus oxychloride is removed at reduced pressure (20–25 mm. with a bath temperature of 55–65°) (Note 4), the receiver being cooled in an ice-salt bath. The red, oily residue is dissolved in 200 ml. of benzene and the benzene and residual phosphorus oxychloride distilled under reduced pressure. This operation is repeated with 200 ml. of fresh benzene to ensure complete removal of phosphorus oxychloride (Note 5). The residue is then cooled to room temperature (Note 6) and is transferred to a 500-ml. pressure-

equalized dropping funnel for immediate use in the following step.

The same 5-l. flask used in the preceding step is used again, without washing; it is fitted with a reflux condenser carrying a drying tube, a sealed mechanical stirrer, and the dropping funnel containing the acid chloride. In the flask are placed 296 g. (4 moles) of dry *tert*-butyl alcohol (Note 7) and 484 g. (4 moles) of dimethylaniline in 600 ml. of anhydrous ether (Note 8). The acid chloride is added dropwise to the stirred solution, the mixture being cooled occasionally with an ice bath to prevent excessive refluxing. After the addition is complete, the reaction mixture is refluxed for 2 hours and then stirred gently at room temperature for 15 hours. Two liters of water is added with stirring, and the mixture is filtered with suction through a Büchner funnel fitted with a matting of glass wool (Note 9). The matting is washed with three 250-ml. portions of ether (Note 10). After separation of the combined ethereal layers, the aqueous layer is extracted twice with 250-ml. portions of ether. The combined ether solutions are washed with successive portions of 2*N* sulfuric acid (a total of 1 l.) until free of dimethylaniline, then with two 200-ml. portions of 2*N* sodium carbonate solution, and dried over sodium carbonate. After removal of the ether by distillation, the residue is transferred to an alkali-washed flask and distilled at reduced pressure through a 20-cm. alkali-washed Vigreux column (Note 11). The yield of colorless product is 355–378 g. (63–67%) boiling at 67–68°/1.5 mm. (90°/10 mm., 54–56°/0.3 mm), $n_D^{20} = 1.4198$.

2. Notes

1. Cyanoacetic acid of 98% purity, obtained from Kay-Fries Chemicals, Inc., was used.

2. A Claisen head with a condenser leading into a flask with a suction arm connected to a drying tube is suitable. Ground-glass joints are recommended.

3. A large bucket containing water and placed on a steam bath serves as a suitable water bath. The temperature is easily controlled between the limits mentioned.

4. The ether is removed from the receiving flask before the phosphorus oxychloride is distilled. A drying tube should be placed between the suction arm of the flask and the water pump, which serves as the source of suction. The reaction mixture may be stirred during the distillation of the oxychloride, or the stirrer may be removed and replaced with a capillary ebulliator tube to which is attached a balloon filled with dry nitrogen.

5. The checkers found that the distillation with benzene ensures a more complete removal of phosphorus oxychloride which, if still present, interferes in the subsequent step and a lower yield of product results.

6. The submitters found that on several occasions, when the residue was not cooled before transfer, it began to generate considerable heat while standing in the dropping funnel and resulted in the total carbonization of the acid chloride.

7. The submitters dried the *tert*-butyl alcohol by refluxing it over calcium hydride overnight and distillation in a moisture-free apparatus. The checkers found that stirring the *tert*-butyl alcohol at 60–70° over calcium hydride for several hours and then distilling the alcohol, using an air condenser, is a satisfactory procedure. When the *tert*-butyl alcohol is refluxed, the alcohol vapors condense and solidify (m.p. 24–25°) in the reflux condenser and cause clogging.

8. These reagents should be weighed out beforehand in order to prevent delay in commencing with this step.

9. The filtration removes some tarry resinous material which would otherwise interfere in the separation of the layers. The checkers found that unless the filtrate is recycled through the same matting several times, to remove practically all the tarry residue, the separation of layers and the subsequent extractions prove troublesome owing mainly to emulsion formation.

10. The checkers found that a considerable amount of product is withheld by the residue on the glass-wool matting. The product is extracted by placing the matting in a beaker, stirring with ether, and filtering. This procedure is repeated twice, and the ether extracts are combined with the original filtrate.

11. The distilling flask and Vigreux column to be used should be washed with 25% aqueous sodium hydroxide solution, rinsed

three times with water, and then dried. Alternatively, about 1 g. of anhydrous potassium carbonate may be added to the residue before distillation.

3. Methods of Preparation

tert-Butyl cyanoacetate has been prepared from *tert*-butyl bromoacetate and potassium cyanide in methanol² and from *tert*-butyl chloroacetate and potassium cyanide in methyl Cellosolve.³ The present method is an adaptation of that of Beech and Pigott⁴ and is similar to the *Organic Syntheses* preparation of *tert*-butyl acetate.⁵

4. Merits of Preparation

The present preparation employs a method of considerable scope which gives much better yields and is considerably less laborious than other methods for the preparation of *tert*-butyl cyanoacetate. The compound is of specific interest since, for example, it may be used in any reaction where ethyl cyanoacetate is used (condensation reactions, etc.), but it has the added advantage that the carbo-*tert*-butoxy group, which may serve in conjunction with the α -cyano group to activate the α -hydrogens (for cyanoethylations, etc.), may be later removed simply by pyrolysis of the compound.

¹ University of Michigan, Ann Arbor, Mich.

² B. Abramovich and C. R. Hauser, *J. Am. Chem. Soc.*, **64**, 2271 (1942).

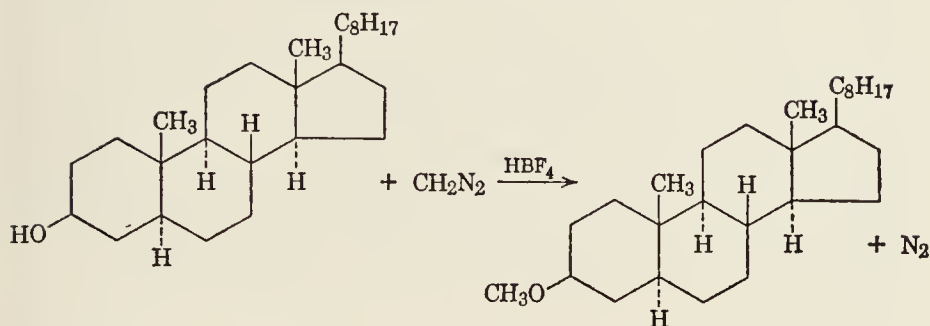
³ Private communication, W. S. Johnson, University of Wisconsin.

⁴ W. F. Beech and H. A. Pigott, *J. Chem. Soc.*, **1955**, 423.

⁵ C. R. Hauser, B. E. Hudson, B. Abramovitch, and J. C. Shivers, *Org. Syntheses*, Coll. Vol. **3**, 142 (1955).

CHOLESTANYL METHYL ETHER

(Cholestane, 3 β -methoxy-)



Submitted by M. NEEMAN^{1,2} and WILLIAM S. JOHNSON.¹

Checked by F. KAPLAN and JOHN D. ROBERTS.

1. Procedure

To a solution of 0.200 g. (0.515 mmole) of dry dihydrocholesterol (Note 1) in 10 ml. of methylene chloride contained in a 50-ml. Erlenmeyer flask is added 0.3 ml. of a catalyst stock solution containing 0.0016 ml. (0.018 mmole) of concentrated fluoboric acid (Note 2) in 3:1 anhydrous diethyl ether-methylene chloride (Note 3). The solution is swirled, and a 0.45*M* solution of diazomethane (Note 4) in dry methylene chloride is added from a buret (Note 5) at a rate of about 2 ml. per minute. The yellow color of diazomethane disappears rapidly on contact with the reaction mixture and nitrogen is vigorously evolved. When about 3 ml. of diazomethane solution has been added, the reaction becomes sluggish. The yellow color persists for several minutes after the total amount of 3.9 ml. of diazomethane solution (1.76 mmoles) has been added (Note 6). After 1 hour the reaction mixture is filtered to remove a small amount of amorphous polymethylene, which is washed with methylene chloride. The washings are combined with the methylene chloride solution, washed with 5 ml. of saturated aqueous sodium bicarbonate, with three

5-ml. portions of water, and dried over anhydrous sodium sulfate. The solvent is removed on a steam bath in a stream of nitrogen and finally at reduced pressure. The crystalline residue of 0.207 g. (Note 7) is recrystallized in a 10-ml. conical flask from 1 ml. of acetone. When the flask has cooled to room temperature, 0.5 ml. of methanol is added, and the flask is chilled to $+2^{\circ}$ for 2 hours. The crystals are collected on a tared Hirsch funnel of 40-mm. diameter, washed on the funnel with two 0.5-ml. portions of ice-cold methanol, and dried for 2 hours at $40^{\circ}/2$ mm. The first crop of cholestanyl methyl ether thus obtained forms large colorless glistening plates, m.p. $85.5\text{--}86^{\circ}$ (Note 8). An additional 0.002 g. of pure methyl ether adheres to the flask and spatula and is collected by washing with acetone. The total first crop material (0.197 g.) represents a 95% yield of methyl ether (Note 9).

2. Notes

1. Satisfactory material of melting point $143\text{--}143.5^{\circ}$ is prepared as already described,³ and dried for 2 hours at $110^{\circ}/2$ mm.

2. Commercial 50% fluoboric acid is evaporated at $50\text{--}60^{\circ}/5$ mm. to afford a residue of about 11*N* total acidity, which is satisfactory for use as a catalyst.

3. The catalyst stock solution should be freshly prepared by placing 19 ml. of anhydrous diethyl ether in a 25-ml. volumetric flask cooled to 0° and adding 0.133 ml. of concentrated fluoboric acid (Note 2). The volume is made up to 25 ml. with methylene chloride.

4. Diazomethane solution in dry methylene chloride may be prepared from N-nitroso-N-methyl-N'-nitroguanidine by a procedure based on McKay's method.⁴ Methylene chloride is substituted for diethyl ether used in the original procedure. A satisfactory solution of diazomethane is obtained, without distilling, by separating the methylene chloride layer from the reaction mixture, drying it for 2 hours over potassium hydroxide pellets, and decanting through a funnel plugged loosely with cotton. The diazomethane solution is kept in a loosely stoppered test tube immersed in a Dewar flask containing Dry Ice during the drying period and prior to use. *All handling of the highly toxic diazo-*

methane should be done in an efficiently exhausted hood. Attention is called to other precautions;⁵ see also pp. 16–17.

Rigorous drying and exclusion of moisture are not necessary. The concentration of diazomethane solutions is determined by analysis,⁵ using about 0.12 g. of benzoic acid per milliliter of solution and assuming a concentration of about 0.8*M* as in McKay's method.^{4b} Solutions approximately 0.45*M* are obtained by appropriate dilution.

5. Burets with ground-glass stopcocks should not be used, as leaking is caused by polymethylene formed preferentially on the ground surfaces. A buret such as "Ultramax F and P," having a stopcock of plastic material, is satisfactory. The buret should be filled immediately before commencement of the reaction to keep the diazomethane solution cool and thus to minimize polymerization. The technique used is very similar to that of a titration, and a number of methylations of prepared batches can be quickly performed with one filling of the buret.

6. Addition of a drop of catalyst stock solution after addition of diazomethane solution is complete causes rapid disappearance of the yellow color. The yield is not affected.

7. The crude reaction product is slightly yellow and has a very faint ammoniacal odor. It may be dissolved in acetone; on slow evaporation to dryness, the solution leaves large glistening transparent plates of good-quality cholestanyl methyl ether, m.p. 83–85°.

8. All melting points are corrected for stem exposure. Reported ⁶ melting point 83°.

9. The mother liquor may be evaporated to dryness and the slightly colored residue recrystallized in a 3-ml. conical flask from 6 drops of 1:1 acetone-methanol. The resulting large plates are easily transferred to a small Hirsch funnel and washed with 5 drops of methanol. This second crop of colorless methyl ether amounts to 0.010 g., m.p. 78.5–79.5°.

3. Methods of Preparation

Cholestanyl methyl ether has been prepared by catalytic hydrogenation of cholesteryl methyl ether ^{6,7} and of cholest-4-en-

3-one in methanolic hydrobromic acid,⁷ and by methylation of cholestanol with methyl iodide in the presence of "activated" silver oxide and sodium hydroxide.⁸ The reported⁹ formation of cholestanyl methyl ether from *epicholestanol* in 96% yield by refluxing with "molecular" potassium in benzene and subsequent treatment with methyl iodide stands unconfirmed.¹⁰ Methanolysis of *epicholestanyl* tosylate afforded a 23% yield of cholestanyl methyl ether.¹¹ The procedure described here,¹² with slight changes in the molar proportions of the reactants, also gave a 98% yield of *epicholestanyl* methyl ether from *epicholestanol*, and a 95% yield of cholesteryl methyl ether from cholesterol.

4. Merits of Preparation

The present procedure is illustrative of the utility of the general method for preparation of methyl ethers from diazomethane and alcohols with fluoboric acid as catalyst.¹²

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² On leave from Technion Israel Institute of Technology, Haifa, Israel.

³ W. F. Bruce and J. O. Ralls, *Org. Syntheses*, Coll. Vol. 2, 191 (1943).

⁴ (a) A. F. McKay, *J. Am. Chem. Soc.*, **70**, 1974 (1948); (b) A. F. McKay et al., *Can. J. Research*, **28B**, 683 (1950).

⁵ F. Arndt, *Org. Syntheses*, Coll. Vol. 2, 165 (1943).

⁶ Th. Wagner-Jauregg and L. Werner, *Z. physiol. Chem.*, **213**, 119 (1932).

⁷ J. C. Babcock and L. F. Fieser, *J. Am. Chem. Soc.*, **74**, 5472 (1952).

⁸ J. L. Dunn, I. M. Heilbron, R. F. Phipers, K. M. Samant, and F. S. Spring, *J. Chem. Soc.*, **1934**, 1576.

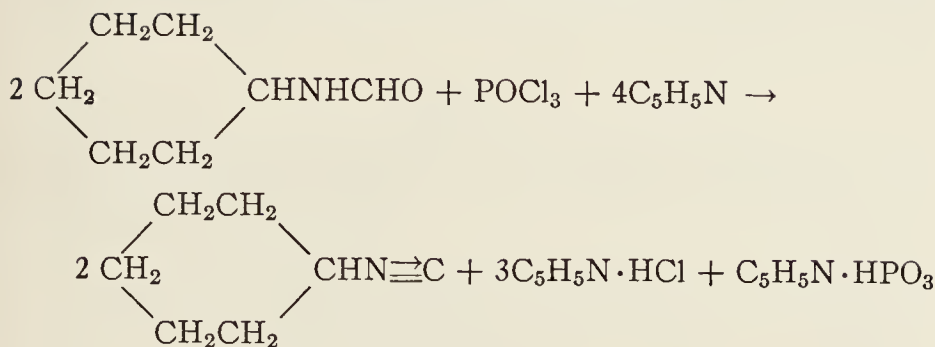
⁹ J. H. Benyon, I. M. Heilbron, and F. S. Spring, *J. Chem. Soc.*, **1937**, 406.

¹⁰ J. R. Lewis and C. W. Shoppee, *J. Chem. Soc.*, **1955**, 1375, have obtained *epicholestanyl* methyl ether under these conditions.

¹¹ H. R. Nace, *J. Am. Chem. Soc.*, **74**, 5937 (1952).

¹² M. C. Caserio, J. D. Roberts, M. Neeman, and W. S. Johnson, *J. Am. Chem. Soc.*, **80**, 2584 (1958); M. Neeman, M. C. Caserio, J. D. Roberts, and W. S. Johnson, *Tetrahedron*, **6**, 36 (1959).

CYCLOHEXYL ISOCYANIDE



Submitted by IVAR UGI, RUDOLF MEYR, MARTIN LIPINSKI,
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Checked by B. C. McKUSICK and M. E. HERMES.

1. Procedure

Caution! Isocyanides should be prepared in a hood since they have unpleasant odors and are toxic.

A solution consisting of 127 g. (1.00 mole) of N-cyclohexylformamide (Note 1), 500 ml. (490 g., 6.2 moles) of pyridine, and 300 ml. of petroleum ether (b.p. 40–60° or 30–60°) is charged into a 2-l., three-necked, round-bottomed flask equipped with a Hershberg stirrer,² dropping funnel, reflux condenser, and thermometer. The flask is immersed in an ice bath, and 92 g. (0.60 mole) of phosphorus oxychloride is added from the dropping funnel to the stirred mixture in the course of 30–40 minutes. The mixture is stirred under reflux for 10 minutes after all the phosphorus oxychloride is added. The mixture is then cooled to 0–5°; this converts it to a heavy slurry. Ice water (800 ml.) is gradually added with stirring, and stirring of the cold mixture is continued until all solid material has dissolved. The organic phase is separated in a separatory funnel. The aqueous phase is extracted with three 60-ml. portions of petroleum ether, and the extracts are combined with the organic phase, which is then extracted with three 100-ml.

portions of water, dried over 20 g. of magnesium sulfate, and distilled through a 40-cm. vacuum-jacketed Vigreux column (Note 2). The petroleum ether is rapidly removed under slightly reduced pressure from a bath at a temperature not exceeding 50–60°. Cyclohexyl isocyanide, a colorless foul-smelling liquid (Note 3), is collected at 56–58°/11 mm.; weight 73–79 g. (67–72%); n_D^{25} 1.4488–1.4501.

2. Notes

1. The checkers prepared N-cyclohexylformamide by slowly adding 260 g. (3.52 moles) of ethyl formate with stirring to 396 g. (4.00 moles) of cyclohexylamine in a flask immersed in an ice bath. After the exothermic reaction ceased, the solution was refluxed for 2 hours and distilled through a 25-cm. Vigreux column to give 403 g. (90%) of N-cyclohexylformamide, b.p. 137–138°/10 mm., n_D^{25} 1.4849.³

2. The checkers used a 50-cm. spinning-band column.⁴ In order to minimize resinification of the cyclohexyl isocyanide, distillation should be as rapid as possible and the temperature in the still pot should not exceed 90°.

3. The disagreeable odor of cyclohexyl isocyanide can be removed from the equipment used in this preparation by washing it with 5% methanolic sulfuric acid solution.

3. Methods of Preparation

Cyclohexyl isocyanide has been prepared only by the dehydration of N-cyclohexylformamide.⁵

4. Merits of Procedure

The present procedure is the best way of preparing aliphatic isocyanides boiling above ethyl isocyanide. It has been applied to the synthesis of the following isocyanides:⁵ isopropyl (38%), *n*-butyl (61%), *tert*-butyl (68%), and benzyl (56%). In preparing isopropyl isocyanide or *tert*-butyl isocyanide, the petroleum ether should be of boiling point 30–35°, as otherwise it is difficult to separate these low-boiling isocyanides in the indicated yield, and,

even then, substantial amounts of isocyanide are found in the petroleum ether fraction.

Aromatic isocyanides can also be prepared conveniently by the dehydration of the corresponding formamides by phosphorus oxychloride, but much better results are obtained if the reaction is done in the presence of potassium *tert*-butoxide rather than pyridine.⁶ Neither method of dehydrating formamides has yet been used to prepare methyl or ethyl isocyanide because their low boiling points make them difficult to isolate from the reaction mixture; hence, until a suitable dehydration procedure is worked out, they are best made by reaction of the corresponding alkyl iodide with silver cyanide.⁷

¹ Institute of Organic Chemistry, University of Munich, Munich, Germany.

² P. S. Pinkney, *Org. Syntheses*, Coll. Vol. 2, 117 (1943).

³ R. WIETZEL, German pat. 454,459 (1928) [*Chem. Zentr.*, 99, I, 2540 (1928)].

⁴ R. G. Nester, *Anal. Chem.*, 28, 278 (1956).

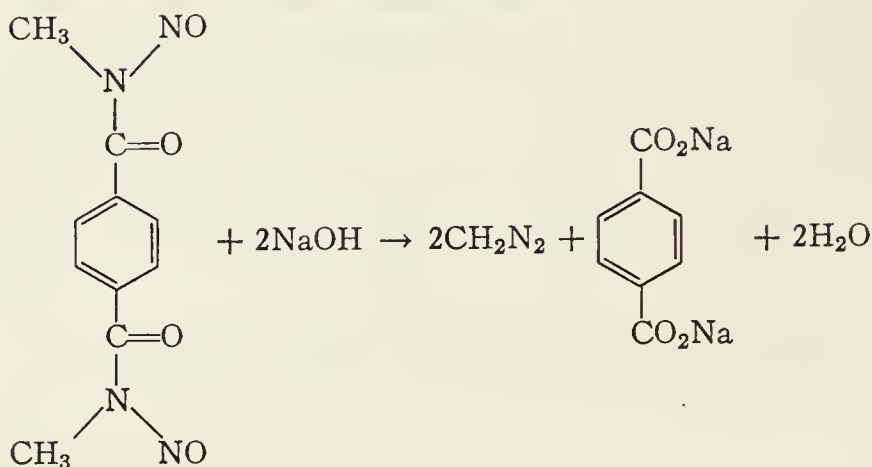
⁵ I. Ugi and R. Meyr, *Chem. Ber.*, 93, 239 (1960).

⁶ I. Ugi and R. Meyr, *this volume*, p. 101.

⁷ H. L. Jackson and B. C. McKusick, *Org. Syntheses*, 35, 62 (1955).

DIAZOMETHANE

(Methane, diazo-)



Submitted by JAMES A. MOORE and DONALD E. REED.¹
 Checked by D. J. PASTO and E. J. COREY.

1. Procedure

Caution! Diazomethane is toxic and explosive. The operation must be carried out in a good hood with an adequate shield (see Note 1).

An efficient condenser (60 cm. or longer) is fitted with an adapter to which is sealed a length of 9-mm. tubing extending nearly to the bottom of a 5-l. round-bottomed flask, which serves as the distillation receiver (Notes 2 and 3). The adapter should be connected to the receiver with a two-hole stopper carrying a drying tube if anhydrous diazomethane is desired. The receiver is placed in a well-mixed ice-salt mixture, and sufficient anhydrous ether (about 200 ml.) is added to cover the tip of the adapter.

In a 5-l. round-bottomed flask are placed 3 l. of U.S.P. solvent grade ether, 450 ml. of diethylene glycol monoethyl ether (Note

4), and 0.6 l. of 30% aqueous sodium hydroxide solution (Note 5). The mixture is chilled in an ice-salt bath to 0° (Note 6), and 180 g. (0.5 mole) of bis-(N-methyl-N-nitroso)terephthalamide (70% in mineral oil) (Note 7) is added in one portion. The flask is immediately transferred to a heating mantle and connected by a gooseneck to the condenser. The yellow color of diazomethane appears in the receiver almost immediately. About 2 l. of ether is distilled in 2–2.5 hours (Note 8); the distilling ether is practically colorless at this point. The tip of the adapter should be kept just below the surface of the distillate during the distillation. The distillate contains 0.76–0.86 mole (76–86%) (Notes 9 and 10) of diazomethane as determined by titration.² When the apparatus has been protected with a drying tube, the diazomethane is suitable for reaction with an acid chloride without further drying.

2. Notes

1. Diazomethane is not only toxic but also potentially explosive. Hence one should wear heavy gloves and goggles and work behind a safety screen or a hood door with safety glass, as is recommended in the preparation of diazomethane described by De Boer and Backer.³ As is also recommended there, ground joints and sharp surfaces should be avoided. Thus all glass tubes should be carefully fire-polished, connections should be made with rubber stoppers, and separatory funnels should be avoided, as should etched or scratched flasks. Furthermore, at least one explosion of diazomethane has been observed at the moment crystals (sharp edges!) suddenly separated from a supersaturated solution. Stirring by means of a Teflon-coated magnetic stirrer is greatly to be preferred to swirling the reaction mixture by hand, for there has been at least one case of a chemist whose hand was injured by an explosion during the preparation of diazomethane in a hand-swirled reaction vessel.

It is imperative that diazomethane solutions not be exposed to direct sunlight or placed near a strong artificial light because light is thought to have been responsible for some of the explosions that have been encountered with diazomethane. Particular caution should be exercised when an organic solvent boiling higher

than ether is used. Because such a solvent has a lower vapor pressure than ether, the concentration of diazomethane in the vapor above the reaction mixture is greater and an explosion is more apt to occur.

Most diazomethane explosions occur during its distillation. Hence diazomethane should not be distilled unless the need justifies it. An ether solution of diazomethane satisfactory for many uses can be prepared as described by Arndt,² where nitrosomethylurea is added to a mixture of ether and 50% aqueous potassium hydroxide and the ether solution of diazomethane is subsequently decanted from the aqueous layer and dried over potassium hydroxide pellets (not sharp-edged sticks!). When distilled diazomethane is required, the alternative procedure of De Boer and Backer³ is particularly good because at no time is much diazomethane present in the distilling flask.

Both the toxicity and explosion hazards associated with diazomethane are discussed by Gutsche.⁴

2. If it is desired to determine the yield of diazomethane by titration, the receiver should be calibrated so that the volume of the distillate can be measured without the necessity of transferring to a graduated vessel.

3. The submitters have used equipment having all connections made with ungreased 29/42 ground-glass joints. This is contrary to previously recommended practice (see Note 1). The submitters feel that ground-glass joints do not represent an added hazard, and that their use expedites the completion of consecutive runs. In the course of many preparations, however, a film of polymethylene was found to accumulate on the joints and prevent a tight fit. This film can be removed by a brief treatment with hot concentrated alkali and vigorous rubbing.

In some forty preparations made by the submitters, one explosion occurred which was attributed to the cracking of the adapter tube during the distillation. The adapter and the drying tube were disintegrated, but the receiver and the contents of the distilling flask were not affected, indicating a local detonation that was not sustained.

The checkers did not use glassware with ground-glass joints. New unmarked flasks and condenser were used which were con-

nected together with fire-polished glass tubing and rubber stoppers.

4. Practical grade 2-(2-ethoxyethoxy)ethanol (Matheson, Coleman and Bell) can be used without further treatment. In a few preparations, the submitters encountered difficulty with the formation of a very stiff gel of disodium terephthalate in the flask during distillation. In one case, this difficulty was traced to the use of an old bottle of 2-(2-ethoxyethoxy)ethanol from another source.

This relatively large volume of cosolvent was found to give optimum yields. The submitters have found that the evolution of diazomethane from a stirred suspension of the reagent in ether and 40% aqueous sodium hydroxide is extremely slow and incomplete.

5. The use of more concentrated solutions of potassium hydroxide gave somewhat lower yields.

6. *Caution! It is extremely important that the flask contents be cooled to at least 0°. The reaction is rapid and a considerable amount of diazomethane is generated at this temperature.*

7. This material is available from the Explosives Department, E. I. du Pont de Nemours and Co., Gibbstown, New Jersey, under the tradename EXR-101. The 30% white mineral oil acts as a stabilizer. The material may be stored indefinitely at room temperature. Details concerning the properties of the compound and recommended precautions in its use are provided in a products bulletin available from the supplier. EXR-101 sometimes turns green on long standing, but this does not affect the yield of diazomethane (private communication from Dr. B. C. McKusick).

8. The yield of diazomethane is slightly lower if the distillation is carried out more slowly.

9. The average yield in some thirty runs was over 80%; yields as high as 95% have been obtained. It is probable that a second receiver in series would permit the recovery of a small additional amount of diazomethane.

10. The checkers decomposed the small amount of diazomethane remaining in the reaction flask by careful addition of 100 ml. of acetic acid before disposal.

3. Methods of Preparation

Diazomethane has been prepared by the action of base on nitrosomethylurea,² nitrosomethylurethane,⁵ N-nitroso- β -methylaminoisobutyl methyl ketone,⁶ *p*-tolylsulfonylmethylnitrosamide,³ and N-nitroso-N-methyl-N'-nitroguanidine.⁷

4. Merits of Preparation

The great advantages of the present method are the availability, moderate cost, and high stability of the nitrosamide, and the suitability for large-scale preparations. The procedure is rapid and simple, and the yields are consistently higher than in any other method tried by the submitters.

¹ Department of Chemistry, University of Delaware, Newark, Del.

² F. Arndt, *Org. Syntheses*, Coll. Vol. 2, 165 (1943).

³ Th. J. De Boer and H. J. Backer, *Org. Syntheses*, 36, 16 (1956).

⁴ C. D. Gutsche, *Org. Reactions*, 8, 391-394 (1954).

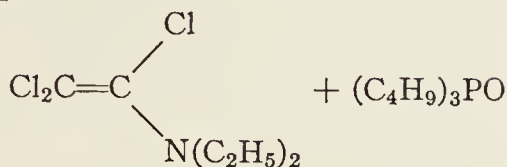
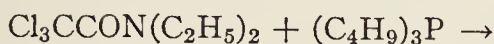
⁵ W. D. McPhee and E. Klingsberg, *Org. Syntheses*, Coll. Vol. 3, 119 (1955).

⁶ C. E. Redemann, F. O. Rice, R. Roberts, and H. P. Ward, *Org. Syntheses*, Coll. Vol. 3, 244 (1955).

⁷ (a) A. F. McKay, *J. Am. Chem. Soc.*, 70, 1974 (1948); (b) A. F. McKay et al., *Can. J. Research*, 28B, 683 (1950).

N,N-DIETHYL-1,2,2-TRICHLOROVINYLAMINE

(Vinylamine, 1,2,2-trichloro-N,N-diethyl-)

Submitted by A. J. SPEZIALE and R. C. FREEMAN.¹

Checked by B. C. McKUSICK and H. D. HARTZLER.

1. Procedure

A. *N,N*-Diethyl-2,2,2-trichloroacetamide. A 1-l. three-necked flask equipped with a stirrer and dropping funnel is charged with 73 g. (1.00 mole) of diethylamine, 500 ml. of ether, and a solution of 40 g. (1.00 mole) of sodium hydroxide in 160 ml. of water. The mixture is stirred and maintained at a temperature of -10° to -15° by a bath of Dry Ice and acetone while 200 g. (1.10 moles) of trichloroacetyl chloride is added in the course of 1 hour. The cooling bath is removed, the temperature is allowed to rise to 10° , and the organic layer is separated. The aqueous layer is extracted with two 50-ml. portions of ether. The ether extracts are combined, washed with 50 ml. of 5% hydrochloric acid, two 50-ml. portions of 5% sodium bicarbonate solution, and 50 ml. of water, and dried over magnesium sulfate. The ether is removed by distillation at atmospheric pressure. The residue is distilled through a short indented Claisen still head at reduced pressure. *N,N*-Diethyl-2,2,2-trichloroacetamide is collected at $77-79^\circ/1.5$ mm.; n_D^{25} 1.4902–1.4912; weight 183–200 g. (84–92%).

B. *N,N*-Diethyl-1,2,2-trichlorovinylamine. The reaction is carried out in a 500-ml. three-necked flask equipped with an efficient mechanical stirrer, a thermometer, a reflux condenser to which a

drying tube containing calcium chloride is attached, and a 250-ml. dropping funnel with a pressure-equalizing tube. The flask is charged with 219 g. (2.00 moles) of N,N-diethyl-2,2,2-trichloroacetamide. A gas-inlet tube is attached to the dropping funnel, and dry nitrogen (Note 1) is passed through the apparatus for 5 minutes with stirring. The gas-inlet tube is removed briefly, 202 g. (2.00 moles) of tri-*n*-butylphosphine (Note 2) is placed in the dropping funnel, the gas-inlet tube is replaced, and nitrogen is passed through the apparatus in a slow stream; the slow flow of nitrogen is continued all during the reaction. The phosphine is added at such a rate that a temperature of 85–90° is reached in 30 minutes (Note 3). The rate of addition is then slowed in order to maintain the temperature within this range. The total addition time is 45–55 minutes.

After all the phosphine has been added, the water bath is replaced by a heating mantle, and the reaction mixture is held at 85–95° for one additional hour and cooled to room temperature. The nitrogen-inlet tube, dropping funnel, and reflux condenser are removed, and the reaction flask is fitted with a 15 x 150-mm. Vigreux column for distillation under reduced pressure. The reaction mixture is then distilled (Note 4). The pot temperature rises from 94° to 150° during the distillation, and the crude N,N-diethyl-1,2,2-trichlorovinylamine, weight 151–164 g., is collected at 73–120°/8–11 mm. Redistillation of the crude vinylamine through a 20 x 400-mm. column packed with glass helices affords 140–150 g. (69–74%) of pure N,N-diethyl-1,2,2-trichlorovinylamine, b.p. 78–79°/18 mm., n_D^{25} 1.4857–1.4867 (Notes 5 and 6).

2. Notes

1. Tri-*n*-butylphosphine reacts exothermically with atmospheric oxygen to form tri-*n*-butylphosphine oxide.

2. Tri-*n*-butylphosphine obtainable from Westvaco Mineral Products, 161 East Forty-second St., New York City, can be used without further purification.

3. Because this reaction is very exothermic, the phosphine should be added cautiously.

4. The reaction and the initial distillation should be carried out on the same day.

5. As N,N-diethyl-1,2,2-trichlorovinylamine reacts rapidly with atmospheric moisture, it should be stored under nitrogen, preferably in a refrigerator.

6. If desired, the tri-*n*-butylphosphine oxide can be recovered by continuing the distillation. Crude tri-*n*-butylphosphine oxide distils at 115–118°/1–2 mm. (pot temperature 125–135°). The pure phosphine oxide² distils at 94–95°/0.03 mm.; m.p. 64.6–66.6°; yield 135–159 g. (62–73%). *Caution! The reaction mixture should not be distilled to dryness.* There should be a residue of about 40–50 ml.

3. Methods of Preparation

N,N-Diethyl-1,2,2-trichlorovinylamine has been prepared by the action of trimethyl, triethyl, or triisopropyl phosphite or triphenylphosphine on N,N-diethyl-2,2,2-trichloroacetamide.³ These methods require a reaction temperature of 150–160° and several distillations in order to obtain a pure product. Consequently, the yields of the vinylamine are lower than by the present procedure.³

4. Merits of Procedure

The procedure has also been applied to the synthesis of N,N-dimethyl-1,2,2-trichlorovinylamine from trichloroacetamide (60% yield),³ and it probably is a general means of preparing N,N-dialkyl-1,2,2-trichlorovinylamines. The reaction is an unusual one involving reduction of the amide and halogen migration and is of theoretical interest.

N,N-Diethyl-1,2,2-trichlorovinylamine undergoes certain reactions which involve the 1-chlorine atom. Acids and alcohols are converted to their respective chlorides. Aniline converts the vinylamine to N,N-diethyl-N'-phenyl-2,2-dichloroacetamidine.³

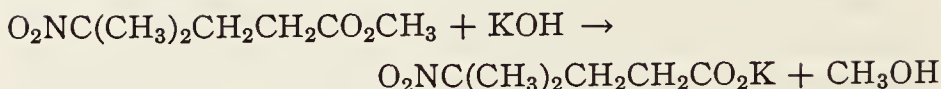
¹ Organic Chemicals Division, Monsanto Chemical Co., St. Louis, Mo.

² G. M. Kosolapoff, *J. Am. Chem. Soc.*, **72**, 5508 (1950).

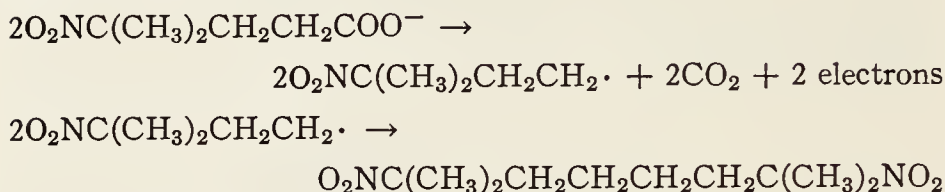
³ A. J. Speziale and R. C. Freeman, *J. Am. Chem. Soc.*, **82**, 903 (1960).

2,7-DIMETHYL-2,7-DINITROOCTANE

(Octane, 2,7-dimethyl-2,7-dinitro-)



Anode Reactions



Cathode Reactions



Submitted by W. H. SHARKEY and C. M. LANGKAMMERER.¹

Checked by MASAOKI TAKAHASHI, MARJORIE C. CASERIO, and JOHN D. ROBERTS.

1. Procedure

A. *4-Methyl-4-nitrovaleric acid*. In a 2-l. three-necked flask equipped with a stirrer and reflux condenser is placed a solution prepared from 118 g. (1.78 moles) of 85% potassium hydroxide pellets and 500 ml. of water. A thermometer may be so placed in the third neck that the bulb extends below the surface of the solution. To this solution is added 300 g. (1.71 moles) of methyl 4-methyl-4-nitrovalerate.² The mixture is stirred and gently heated (Notes 1 and 2). After hydrolysis has started, as indicated by changes in appearance of the hazy reaction mixture, the external source of heat is removed. The reaction is complete when the cloudy mixture has changed to a clear solution. This requires about 20–25 minutes (Note 3).

The reaction mixture is cooled to room temperature, and a saturated solution of potassium permanganate is added in an amount sufficient for a violet color to persist for about 1 minute

before turning green (Note 4). About 100–110 ml. is required. Manganese dioxide is removed by filtration, and the filtrate is extracted with methylene chloride to remove non-acidic organic material. The aqueous layer is acidified with 18% hydrochloric acid, whereupon a pale yellow or green oil separates as a bottom layer. The oil is removed, and the aqueous layer is washed with methylene chloride. The washings are added to the oil, and the combined product is dried with anhydrous magnesium sulfate. Methylene chloride is removed by distillation, and the residual oil is distilled under reduced pressure through a 6-in. Vigreux column (Note 5). The fraction boiling at 125–135° (0.9–1.5 mm.) amounts to 217–225 g. (79–82%) and is a colorless oil that crystallizes on standing or when seeded to give a solid with a melting point of approximately 35–45°. This fraction is redistilled through a 24-in. spinning-band column and gives 166–180 g. (60–65%) of colorless 4-methyl-4-nitrovaleric acid, b.p. 122–124°/0.70–0.90 mm., m.p. 45–46° (Note 6).

B. *2,7-Dimethyl-2,7-dinitroöctane*. A 200-mm. desiccator is adapted for use as an electrolysis cell. A lid is prepared from a glass plate ground to fit the desiccator; holes are bored in the lid to accommodate electrodes, a thermometer, and a stirrer, and to provide an opening for making additions to the cathode compartment. The cathode (Note 7) is placed in a porous ceramic cup having outside dimensions 4 in. deep, 6 in. long, and 2 in. wide (Note 8). This cup is placed on the glazed ceramic plate of the desiccator under the holes cut in the lid for the cathode and for making additions. The glazed ceramic plate is notched so that it can be slipped down over the supports in the bottom of the desiccator. The notches should be large enough for the ceramic plate to be about halfway between its normal position and the bottom of the desiccator (Note 9). The cathode is a 26-gauge stainless-steel plate 3 in. square (Note 10), and the anode consists of two platinum plates each 0.01 in. thick and 3 in. square (Note 11) placed as close as possible, one on either side, to the ceramic cup without touching the sides of the cup.

A solution made by dissolving 161 g. (1 mole) of 4-methyl-4-nitrovaleric acid and 33.0 g. (0.5 mole) of potassium hydroxide in 2.7 l. of methanol is added to the cell. The ceramic cup is filled

with 200 ml. of 2*N* potassium hydroxide in methanol. The cell contents are cooled to 20° (Note 12), and current is passed through the solution (Note 13). When the current is turned on, vigorous evolution of hydrogen takes place inside the porous cup. Potassium hydroxide (2*N*) in methanol is added as needed to maintain the original volume inside the cup (Note 14). Carbon dioxide is evolved at the anodes. After about 5 hours, white crystals of the dinitroöctane form in the anode solution. As electrolysis proceeds, the resistance of the cell increases, and after several hours the cell is operated at 3–5 amperes and 60–80 volts. If a current of 3–5 amperes cannot be maintained, it is desirable to add 2*N* potassium hydroxide in methanol to the anode compartment (Notes 15 and 16). After 8 hours of operation, the current is shut off, the ceramic cup removed and cleaned, and the anode solution cooled to about –30°. The anode solution is filtered to remove crystals of 2,7-dimethyl-2,7-dinitroöctane. The yield of dry product, m.p. 98–100°, amounts to 50–65.5 g. (43–56%), which is sufficiently pure for most uses (Note 17). One recrystallization from methanol (Note 18) gives pure 2,7-dimethyl-2,7-dinitroöctane, m.p. 100–101° (lit.³ 101.5–102°).

2. Notes

1. If stirring is not used, hydrolysis does not start until the reaction mixture is heated almost to the reflux temperature. Under these conditions the reaction, which is exothermic, proceeds so rapidly that the reflux condenser is flooded.

2. Although no explosions have yet occurred, it is advisable to conduct this reaction behind a shield. The hydrolysis, once started, proceeds quite rapidly.

3. The time required varies with the initial temperature of the hydrolysis solution. With warm solutions, e.g., freshly made potassium hydroxide solution, external heating is not needed. With such a solution, the checkers found that a cloudy mixture having an initial internal temperature of 40° became clear within 2–5 minutes of mixing and during this time the temperature rose to 70°. Stirring was continued for 20 minutes to ensure complete hydrolysis.

4. Addition of potassium permanganate removes colored impurities that otherwise persist through subsequent distillations of the acid. The maximum concentration of potassium permanganate in water at room temperature is about 5%. It may be more convenient to use a concentrated solution of sodium permanganate, which is very soluble in water. However, the end point is difficult to observe with sodium permanganate.

5. During this first distillation, nitrogen oxides are evolved in appreciable amounts. It is suggested this operation be done behind a shield in a well-ventilated area. A trap cooled with a mixture of solid carbon dioxide and acetone or with liquid air should be inserted between the column and the vacuum pump. Pumps used in this distillation did not appear to suffer corrosion damage. A dry oil was used and changed after each distillation.

6. It may be necessary in this second distillation to apply a source of heat to the fraction-collecting system to prevent crystallization of the product prior to entry of the distillate into the receivers.

7. The cathode is the electrode connected to the negative terminal of the current source.

8. A satisfactory alumina cup may be purchased from the Norton Company, Worcester, Mass., Catalog No. 44805, RA-98.

9. This is necessary because the top of the porous cup must be below the lip of the desiccator. The volume of the desiccator up to the top of the porous cup should be 4 l.

10. The considerable heat generated inside the cup leads to rapid evaporation of the methanol with which the cup is filled. The cell can be operated by constant replenishment of methanol. However, loss of methanol can be minimized by use of a water-cooled cathode. Such an electrode is conveniently prepared from two 3-in.-square stainless-steel plates and a strip of stainless steel about 0.25 in. wide, which are welded to form a stainless-steel box. Nipples serving as water inlet and outlet are welded to the top of the box.

11. The 3-in.-square platinum plates are welded to a heavy platinum wire that protrudes through one of the holes cut in the glass lid. Heavy copper wire (No. 10) is used to connect the electrodes to the source of current.

12. This temperature is easily maintained by surrounding the cell with a methanol bath cooled with solid carbon dioxide. About 100 lb. of solid carbon dioxide is required for 8 hours' operation. Yields are severely reduced if the methanol is allowed to boil. Temperatures lower than 20° can be used but are less satisfactory.

13. The initial current is usually 6–8 amperes at 50–60 volts. The resistance of the cell constantly changes because of depletion of electrolyte and deposition of potassium methoxide in the pores of the ceramic cup. The preferred source of current is a rectifier capable of delivering 10–15 amperes at 30–90 volts. Lead storage batteries connected in series are also satisfactory but require frequent recharging.

14. In a typical run, 30 ml. of 2*N* potassium hydroxide in methanol was added at the end of each hour of operation. Total addition was 210 ml.

15. The amount added must be less than that required to bring the pH to 7. When the pH of the anode solution is greater than 7, undesirable reactions occur.

16. The checkers found that after 5.5 hours the current dropped below 3 amperes at 75 volts. Addition of 25 ml. of 2*N* potassium hydroxide in methanol to the anode solution increased the current to 6 amperes. Subsequent additions of 10–15 ml. of base were made approximately every 30 minutes. The total volume of base added was 80 ml.

17. Some unchanged 4-methyl-4-nitrovaleric acid can be recovered from the spent electrolysis solution by alkaline extraction followed by acidification and distillation of the water-insoluble oil. However, under ordinary circumstances, recovery of this material is not worth the effort expended.

18. About 500 ml. of refluxing methanol and 58 g. of crude product afford about 53 g. (95% recovery) of recrystallized material.

3. Methods of Preparation

2,7-Dimethyl-2,7-dinitrooctane has been prepared by nitration of 2,7-dimethyloctane.³

4. Merits of Preparation

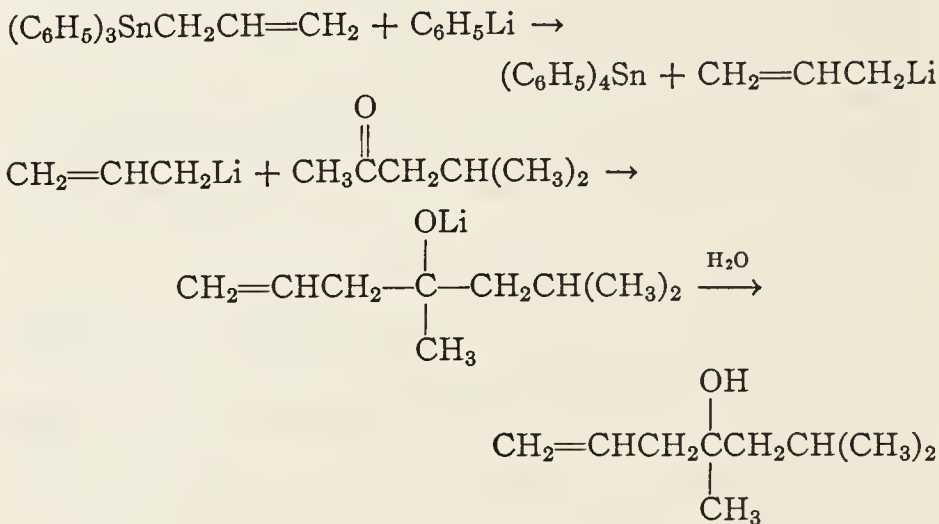
Kolbe electrolysis is generally useful for the formation of hydrocarbons from monocarboxylic acids and for the preparation of many difunctional compounds as well. A specific illustration is the synthesis of esters of long-chain dicarboxylic acids from monoesters of appropriate dicarboxylic acids (see p. 33). A number of these syntheses are discussed by Fichter.⁴ In the present preparation, a two-compartment cell is employed to avoid, or at least greatly reduce, undesired reduction of the nitro group at the cathode. It seems likely that the procedure could be adapted to the preparation of other difunctional compounds containing groups that are easily reduced.

¹ Contribution No. 516 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Co., Wilmington, Del.

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³ M. Konowalow, *J. Russ. Phys.-Chem. Soc.*, **38**, 124 (1906) [*Chem. Zentr.*, **1906**, II, 314].

⁴ F. Fichter, *Organische Elektrochemie*, p. 17, Theodor Steinkopff, Dresden and Leipzig, 1942.

4,6-DIMETHYL-1-HEPTEN-4-OL**(1-Hepten-4-ol, 4,6-dimethyl-)**

Submitted by DIETMAR SEYFERTH and MICHAEL A. WEINER.¹
 Checked by MELVIN S. NEWMAN and CLIFFORD Y. PEERY.

1. Procedure

A solution of 50 g. (0.127 mole) of allyltriphenyltin (Notes 1 and 2) in 200 ml. of diethyl ether (Note 3) is prepared in a 1-l. three-necked flask fitted with a reflux condenser, a motor-driven glass sleeve-type stirrer, nitrogen-inlet tube, and a 250-ml. dropping funnel with pressure-equalizing side arm. After the system has been flushed thoroughly with prepurified nitrogen, 113 ml. of a 1.13*N* solution of phenyllithium (0.127 mole) in diethyl ether (Note 4) is added rapidly to the stirred allyltriphenyltin solution. Precipitation of tetraphenyltin occurs immediately, and the reaction mixture is stirred for 30 minutes in an atmosphere of prepurified nitrogen. Through the dropping funnel is then added 12.0 g. (0.12 mole) of 4-methyl-2-pentanone (Note 5) in 25 ml. of diethyl ether at such a rate that moderate reflux is maintained. Subsequently the reaction mixture is refluxed for 1 hour, allowed

to cool to room temperature, and hydrolyzed by adding 100 ml. of distilled water (Note 6). The solid tetraphenyltin is filtered (53.5 g. = 98% yield), and the filtrate is transferred to a separatory funnel. The aqueous layer is separated and extracted with three 30-ml. portions of ether. The ethereal extracts and the organic layer are combined and dried over anhydrous magnesium sulfate. After removal of the ether by distillation at atmospheric pressure, the residue is filtered through a sintered-glass funnel into a 250-ml. distilling flask and fractionally distilled at reduced pressure using a vacuum-jacketed Vigreux column equipped with a still head of the total-condensing, partial-takeoff type. 4,6-Dimethyl-1-hepten-4-ol, b.p. 70–71°/20 mm., n_D^{20} 1.4403, is obtained in 70–75% yield (12.0–12.8 g.) (Note 7).

2. Notes

1. Allyltriphenyltin is prepared as follows. To a 3-l. three-necked flask fitted with a reflux condenser, a motor-driven stirrer, nitrogen-inlet tube, and a 1-l. dropping funnel with pressure-equalizing side arm are added 50 g. (2.1 g. atom) of magnesium turnings and 800 ml. of diethyl ether (Mallinckrodt reagent grade). The dropping funnel is charged with a solution of 120 g. (1.0 mole) of allyl bromide (Eastman Kodak white label) and 250 g. (0.65 mole) of triphenyltin chloride (Metal Thermit Corporation) in 600 ml. of tetrahydrofuran (Electrochemicals Department, E. I. du Pont de Nemours and Company, Inc.) which has been freshly distilled from lithium aluminium hydride. This solution is added to the vigorously stirred, refluxing magnesium suspension during 7 hours. After the addition is complete, 500 ml. of dry benzene is added and the reaction mixture is refluxed overnight at 60°. It is then hydrolyzed by careful addition of 150 ml. of a saturated ammonium chloride solution. The organic phase is decanted from the solids, and the latter are washed twice with ether. The combined organic layer and ethereal extracts are evaporated at reduced pressure with the aid of a rotary evaporator. The solid residue is recrystallized from 350 ml. of ligroin. The yield of product, m.p. 73–74°, is 190–205 g. (75–80%).

Allyltriphenyltin can also be prepared by using the reaction of preformed allylmagnesium bromide with triphenyltin chloride.² However, the submitters prefer the simpler procedure described above for large-scale preparations of allyltin compounds.

2. Tetraallyltin, triallylphenyltin, and diallyldiphenyltin may be used in place of allyltriphenyltin.

3. The diethyl ether used is Mallinckrodt reagent grade and is distilled from lithium aluminum hydride before use.

4. Ethereal phenyllithium, prepared from lithium and bromobenzene,³ may be standardized by adding an aliquot to water and titrating with standard sulfuric acid.

5. The 4-methyl-2-pentanone used is Eastman Kodak white label grade.

6. The first few milliliters of water should be added dropwise.

7. The reported ⁴ physical constants for 4,6-dimethyl-1-hepten-4-ol are b.p. 68–69°/20 mm., n_D^{20} 1.4402.

3. Methods of Preparation

This procedure is essentially that reported previously.⁵ 4,6-Dimethyl-1-hepten-4-ol has also been prepared by the reaction between allylmagnesium bromide and 4-methyl-2-pentanone,⁴ by the treatment of magnesium with a mixture of allyl bromide and 4-methyl-2-pentanone,^{6,7} and by the treatment of zinc with a mixture of allyl iodide and 4-methyl-2-pentanone.⁸

4. Merits of Preparation

The present synthesis of 4,6-dimethyl-1-hepten-4-ol is an example of the preparation and use of allyllithium, hitherto unknown as a pure reagent. The same general procedure may be used to prepare vinylolithium from ether solutions of any of the compounds $(CH_2=CH)_nSn(C_6H_5)_{4-n}$ ($n = 1-4$),⁹ and benzylolithium from any of the $(C_6H_5CH_2)_nSn(C_6H_5)_{4-n}$ ($n = 1-4$) compounds.¹⁰

Allyllithium is of particular value in the preparation of allyl-metal derivatives.⁵

¹ Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Mass. Supported by the National Science Foundation under Grant G7325.

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⁵ D. Seyferth and M. A. Weiner, *J. Org. Chem.*, **24**, 1395 (1959).

⁶ A. Knorr, Ger. pat. 544,388 (1930) [*C.A.*, **26**, 2466 (1932)].

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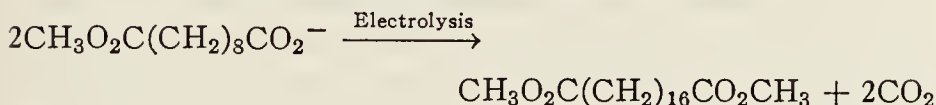
⁸ D. Marko, *J. prakt. Chem.*, [2] **71**, 258 (1905).

⁹ D. Seyferth and M. A. Weiner, *Chem. & Ind. (London)*, **1959**, 402.

¹⁰ H. Gilman and S. D. Rosenberg, *J. Org. Chem.*, **24**, 2063 (1959); D. Seyferth and C. R. Sabet, unpublished.

DIMETHYL OCTADECANEDIOATE

(Octadecanedioic acid, dimethyl ester)



Submitted by SHERLOCK SWANN, JR., and W. E. GARRISON, JR.¹

Checked by JAMES CASON, JOHN A. CARLSON, and STANLEY WOOD.

1. Procedure

To 500 ml. of absolute methanol (Note 1) in a 1-l. electrolytic (tall form) beaker is added 1.1 g. (0.05 g. atom) of clean sodium metal. After solution of the sodium, 216 g. (1.0 mole) of methyl hydrogen sebacate (Note 2) is dissolved in the sodium methoxide solution. A magnetic stirring bar is placed in the beaker which is then fitted with a large neoprene stopper (Note 3) holding a platinum sheet anode, 12 cm.² in area; and two platinum sheet cathodes, approximately 5.3 cm.² in area, spaced equidistantly on either side of the anode at a distance of approximately 1.5 cm. (Note 4). The stopper is also provided with a stoppered entry tube and an efficient reflux condenser (Note 5).

The electrodes are connected to a suitable variable source of direct current (Note 6), the magnetic stirrer is started, and a potential of about 50 volts is applied. This results in a current flow of 1–2 amperes. The solution soon comes to boiling; the voltage is then regulated so that a rapid reflux is maintained (Note 7).

Completion of the run, after 30–40 hours, is indicated when a few drops of the solution show an alkaline reaction to phenolphthalein. No harm is done if the electrolysis is carried a few hours beyond this point; however, after excessively long periods, formation of polymeric material lowers the yield and renders purification of the product rather troublesome.

Upon completion of the reaction (Note 8) the solution is acidified with acetic acid, and the solvent removed under reduced pressure. The residue is dissolved in about 1.4 l. of ether and filtered into a 2-l. separatory funnel through fluted paper. After the ether solution has been washed with two 300-ml. portions of 5% aqueous sodium bicarbonate solution (Note 9), the ether is removed on a steam bath. The residue is dissolved in about 1.5 l. of warm methanol, and the solution is allowed to cool to room temperature. The crystallized product is collected by suction filtration on a Büchner funnel and pressed well. The product is rather waxy and is best washed by transferring it to a beaker and stirring thoroughly with about 150 ml. of cold methanol. The white crystals are then collected and pressed well again. If the filtrate is colored, the crystals are washed again with a smaller quantity of methanol. The combined filtrate and washings are concentrated to one-half the original volume and chilled in ice to yield a few grams of additional product of the same melting point. The combined lots are dried in a vacuum desiccator. The yield amounts to 116–126 g. (68–74%) of white, microcrystalline dimethyl octadecanedioate, m.p. 57–58°.

2. Notes

1. Analytical reagent absolute methanol is sufficiently pure for this purpose.

2. The methyl hydrogen sebacate used by the submitters was prepared by the method described by Pattison and co-workers,²

which is a modification of the method described in *Organic Syntheses*, Coll. Vol. 2, 276 (1943), for ethyl hydrogen sebacate. The methyl rather than the ethyl ester is preferred because of the greater ease of purification of methyl hydrogen sebacate and dimethyl octadecanedioate. The checkers prepared methyl hydrogen sebacate by the convenient procedure which has been described for methyl hydrogen hendecanedioate.³ Absence of diacid in the half ester is imperative, for each molecule of diacid (in low concentration) will couple with two molecules of half ester.

3. A rubber stopper will suffice, but neoprene is more durable.

4. Convenient dimensions are 3 x 4 cm. for the anode, and 2.3 x 2.3 cm. for the cathode. The bottom of the anode should extend to about 3 cm. from the bottom of the beaker, and the centers of the cathodes should be lined up with the center of the anode. The submitters and checkers used 0.002-in. platinum sheet. Thinner material is easily distorted by the action of the stirrer and may thus develop a short circuit. Platinum wire may be attached to the sheet by heating both parts to redness and hammering them together. The wire may then be sealed in a piece of Pyrex tubing, which is passed through a properly located hole in the stopper, and mercury is used to make contact with the lead-in wire.⁴

In a run one-half the size here described, the checkers obtained similar results by using the same geometry of electrodes with the same concentrations of reactants in a 700-ml. tall-form beaker, with one-half the electrolysis time.

5. It is most convenient to insert a 24/40 outer joint in the stopper to accommodate the condenser. A 14/20 outer joint makes a convenient entry tube for withdrawing samples in order to determine when alkalinity has been reached. This joint must be stoppered during the electrolysis, which is under reflux.

6. A variable field d-c motor generator was used by the submitters. In lieu of such equipment, the checkers used a 120-volt d-c source with a heavy-duty resistor in the circuit. Occasionally, a film of polymeric material may form on the anode and reduce the current flow. This condition may be corrected by reversing the current flow for a period of 5-10 seconds. A suitable control circuit is diagrammed in Fig. 1.

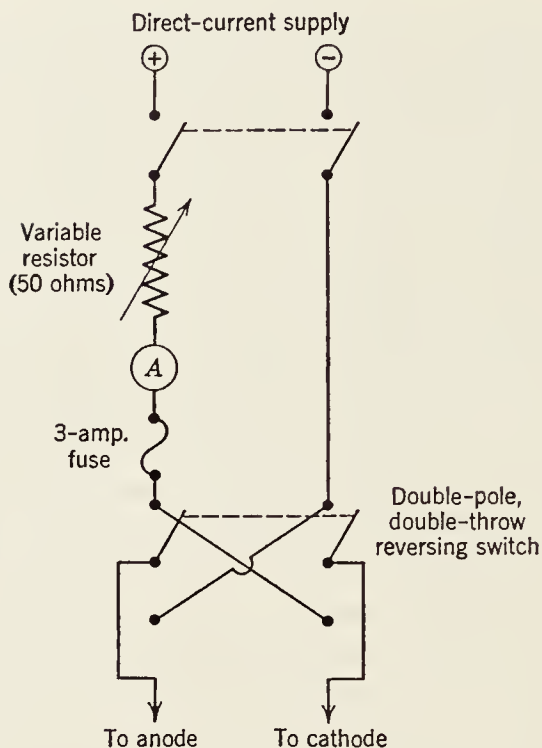


FIG. 1

7. It is usually necessary to increase the applied voltage toward the end of the electrolysis in order to keep the current flow at a high rate. The submitters usually finished the electrolysis at 140 volts; however, the checkers found that a limit of 120 volts resulted in no significant delay in completion of the electrolysis.

8. The electrodes should be removed promptly from the warm reaction mixture, for the solution sets to a solid mass on cooling. It is most convenient to proceed with work-up of the warm solution.

9. An insignificant amount of half ester is recovered by acidification of the bicarbonate washings, followed by extraction with ether.

3. Methods of Preparation

Dimethyl and diethyl octadecanedioate have been prepared by the electrolysis of the sodium or potassium salts of methyl or ethyl hydrogen sebacate in water⁵ or in methanol.⁶

4. Merits of Preparation

The advantages of this preparation of dimethyl octadecanedioate over that described earlier⁵ are purity of product, no foaming of the electrolyte, higher yields, and elimination of the use of large quantities of the salt of the acid ester as supporting electrolyte. The procedure is regarded as near the optimum for a Kolbe electrolysis.

¹ Department of Chemistry, University of Illinois, Urbana, Ill. This work was supported by a grant from the National Science Foundation for polymer research.

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³ L. J. Durham, D. J. McLeod, and J. Cason, *Org. Syntheses*, **38**, 55 (1958).

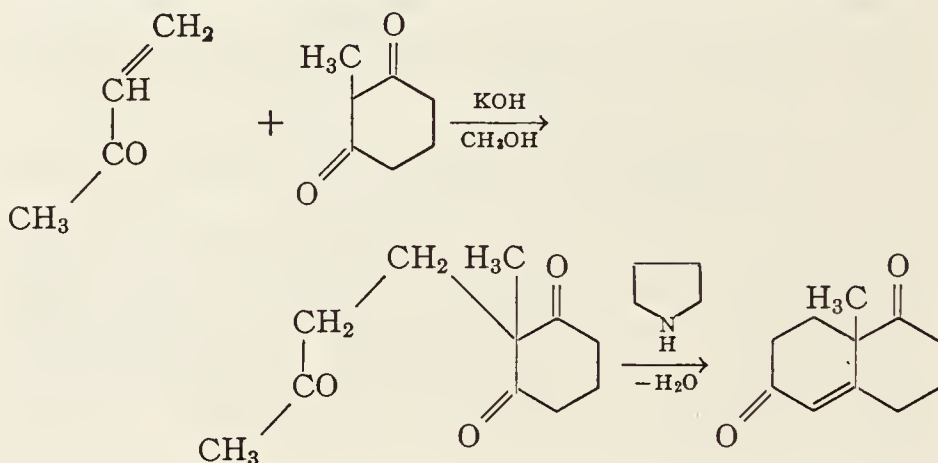
⁴ S. Swann, Jr., in Weissberger, *Technique of Organic Chemistry*, Vol. 2, 1950, 2nd ed., p. 400, Interscience, New York.

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1,6-DIOXO-8a-METHYL-1,2,3,4,6,7,8,8a-OCTAHYDRONAPHTHALENE

(1,6-Naphthalenedione, 1,2,3,4,6,7,8,8a-octahydro-8a-methyl-)



Submitted by S. RAMACHANDRAN and MELVIN S. NEWMAN.¹

Checked by MAX TISHLER, G. A. STEIN, and G. LINDBERG.

1. Procedure

A mixture of 63.1 g. (0.5 mole) of 2-methyl-1,3-cyclohexanedione (Note 1), 52.6 g. (0.75 mole) of methyl vinyl ketone (Note 2), about 0.25 g. (3 pellets) of potassium hydroxide, and 250 ml. of absolute methanol is placed in a 500-ml. round-bottomed flask fitted with a reflux condenser and a drying tube (Note 3). The mixture is heated under reflux for 3 hours, and the dione gradually goes into solution. At the end of this period, methanol and the excess methyl vinyl ketone are removed by distillation under reduced pressure (Notes 4 and 5). The residual liquid is dissolved in 250 ml. of benzene, a Dean-Stark phase-separating head is attached, and 20 ml. of solvent is removed by distillation at atmospheric pressure to remove traces of water and methanol. The solution is cooled well below the boiling point, 3 ml. of

pyrrolidine is added (Note 6) and the mixture held at reflux for about 30 minutes, during which time about 9 ml. of water collects in the trap. Refluxing is continued for an additional 15 minutes after the separation of water ceases. The water collected is removed, and then 50 ml. of solvent is distilled. The reddish reaction mixture is cooled to room temperature and diluted with 150 ml. of ether. This solution is washed with 100 ml. of distilled water containing 15 ml. of 10% hydrochloric acid and 100 ml. of water. The aqueous extracts are extracted with 50 ml. of ether (Note 7), and the combined organic layers are washed with three 100-ml. portions of water, then with saturated salt solution and dried over magnesium sulfate. The solvents are then removed, and on distillation of the residue (82–85 g.) (Note 8) at 0.5–1.0 mm. (Note 9) the material, b.p. 117–145°, is collected and diluted with 5 ml. of ether. The distillate is placed overnight in a refrigerator, the resulting crystals are then collected by rapid filtration and washed with about 25 ml. of cold ether (Notes 10 and 11). The first crop of diketone weighs 50–53 g. and is colorless. The combined mother liquors are redistilled to obtain a further 4–6 g. of crystalline product. A yield of 56–58 g. (63–65% based on dione) of 1,6-dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, m.p. 47–50°, suitable for most other purposes, is obtained (Note 12).

2. Notes

1. The 2-methyl-1,3-cyclohexanedione was prepared by the method described by Mekler et al., this volume, p. 56.

2. Technical grade methyl vinyl ketone supplied by Matheson, Coleman and Bell Co., Cincinnati, Ohio, was used without further purification.

3. The checkers found that stirring during reflux and concentration and in the cyclization step was advantageous.

4. The submitters report that the intermediate 2-methyl-2-(3'-oxobutyl)-1,3-cyclohexanedione can be isolated in 85% yield² at this point if desired.

5. The checkers removed methanol and methyl vinyl ketone at 650 mm. pressure with a water bath at 70°.

6. On adding pyrrolidine an exothermic reaction occurs rapidly. Cooling is needed to prevent too rapid a reaction. The submitters report that piperidine may be used in place of pyrrolidine.

7. The checkers extracted the aqueous extracts twice with 75-ml. portions of ether.

8. The checkers found the residual weights to amount to 87–100 g.

9. The checkers used a saddle-packed 5-in. column and found b.p. 137–150°/0.6–0.7 mm.; 123–150°/0.2–0.5 mm.; and 132–141°/0.5–0.8 mm.

10. A successful crystallization yields relatively large crystals which may be rapidly filtered and washed with ether with little loss. If fine crystals are obtained, it is preferable to redissolve and allow the material to crystallize again.

11. Because of the high solubility in ether (1 g. per 2.5 ml. at room temperature), the checkers washed the product with hexane (b.p. 60–71°).

12. Purer product, m.p. 48.6–50.0°, may be obtained by crystallization from ether.

3. Methods of Preparation

1,6-Dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene has been obtained through the reaction of 2-methyl-1,3-cyclohexanedione with acetonedicarboxylic acid and formaldehyde,³ 4-diethylamino-2-butanone methiodide,³ pyridine and 4-diethylamino-2-butanone,⁴ triethylamine and 4-diethylamino-2-butanone,⁵ and by cyclization of 2-methyl-2-(3-oxobutyl)-1,3-cyclohexanedione using either aluminum *tert*-butoxide or piperidine phosphate as catalyst.^{6,7}

4. Merits of Preparation

1,6-Dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene has been employed as an intermediate in the synthesis of terpenes^{8,9} and in the projected synthesis of steroids.^{4,10}

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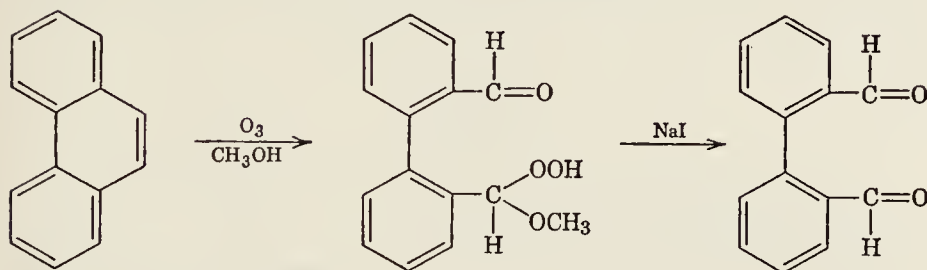
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DIPHENALDEHYDE

(Biphenyl, 2,2'-diformyl-)

Submitted by PHILIP S. BAILEY and RONALD E. ERICKSON.¹

Checked by MARJORIE C. CASERIO and JOHN D. ROBERTS.

1. Procedure

A finely divided suspension (Notes 1 and 2) of 10.0 g. (0.056 mole) of phenanthrene (Note 3) in 200 ml. of dry methanol (Note 4) is placed in a standard ozonolysis vessel (Note 5). The reaction mixture is cooled in a Dewar flask by an acetone-Dry Ice mixture to about -30° (Notes 6 and 7), and ozone (Note 8) is passed through at a rate of about 20 l. per hour (Note 9) until all the phenanthrene has reacted (Note 10).

To the cooled reaction mixture are added 25–30 g. (roughly 1.5 times the theoretical 0.112 mole) of sodium or potassium iodide and 30 ml. of glacial acetic acid (Note 11). After the addition, the reaction mixture is allowed to stand at room temperature for

30 minutes to 1 hour. The released iodine is reduced with 10% sodium thiosulfate solution, after which the reaction mixture is placed immediately under an air blast (Note 12). As the methanol evaporates, the product begins to crystallize (Note 13). The crystallization should be well advanced by the time most of the methanol has evaporated. Water is then added, and the solid is removed by filtration and dried. The yield of crude product, softening at about 54° and melting at 59–62°, is 9.2–11.4 g. (78–96%). The crude product may be recrystallized by dissolving it in the minimal amount (40–50 ml.) of dry ether and slowly adding about 150 ml. of ligroin (Note 14). Small crystals separate halfway through the addition, and crystallization is completed by cooling the mixture in an acetone-Dry Ice bath. An 80–90% recovery of pale yellow crystals melting at 62–63° is obtained. A second recrystallization from 70% aqueous ethanol gives nearly colorless crystals melting at 62.5–63.5° (Note 15).

2. Notes

1. This is produced by dissolving the phenanthrene in the refluxing solvent and cooling rapidly.

2. The finely divided suspension is necessary in order for the phenanthrene to go into solution and react readily during the ozonolysis.

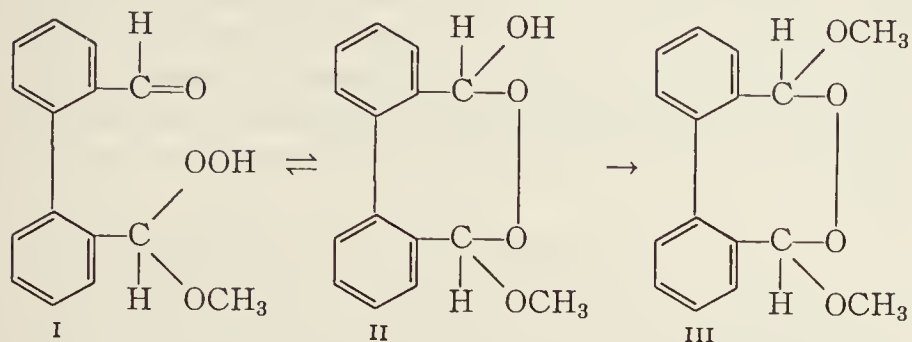
3. Eastman white label 599, m.p. 99–100°, was used.

4. Commercial methanol reagent containing 0.1% or less of water is satisfactory.

5. The usual long, cylindrical, gas-absorption-type vessel with an inlet tube extending to near the bottom is satisfactory.² The total volume of the vessel should be at least twice that of the reaction solution. More elaborate reaction vessels equipped with a stirrer³ are very useful in reactions such as this in which the reactant is suspended in the solvent. However, the commercially available vessels of this type are not large enough for the reaction mixture described here.

6. The temperature of the reaction mixture should not be allowed to rise above –20°, because at higher temperatures ozone tends to react with the solvent and the reactions shown below

also occur. Compound III is not readily reduced to the dialdehyde.



7. Compound II may precipitate during ozonolysis at -30° or below. This is in no way detrimental.

8. A Welsbach T23 ozonator was used by the submitters. Oxygen dried by a Pittsburg Laboratory-Lectrodryer to a dew point of -60° was passed through the ozonator, which was set to produce a 5-6% by weight concentration of ozone.⁴ Following the ozonation flask were a potassium iodide trap and a wet-test meter.⁴ The checkers used a simple ozonator capable of producing 3.8% by weight of ozone at a flow rate of 20 l. per hour from oxygen dried by passage through a 30-cm. column of silica gel.

9. The rate should be sufficiently great to cause considerable agitation of the suspended phenanthrene. As the reaction proceeds, the reaction vessel should be shaken frequently in order to maintain good contact between the phenanthrene and ozone. For smaller runs a reaction vessel that includes a stirrer is advantageous (Note 5).

The checkers found it convenient to use leads of Tygon tubing of sufficient length to allow the reaction flask to be withdrawn at intervals from the Dewar flask and shaken manually.

10. Unreacted ozone starts passing through to the potassium iodide trap toward the end of the reaction. However, it is best to continue the reaction until all the suspended phenanthrene has disappeared. This usually requires a total of 1.1-1.3 mole-equivalents of ozone. Unless all the phenanthrene has reacted, difficulty is encountered in the crystallization and/or recrystallization of the dialdehyde.

11. The reduction may be carried out in the ozonolysis flask, or the reaction mixture may be transferred first to an Erlenmeyer flask or beaker. The iodide and acetic acid should be added simultaneously. The reaction of peroxides with iodide ion is exothermic. The temperature of the reaction mixture should be kept below -20° while the sodium iodide and acetic acid are added, after which it may be allowed to rise slowly to room temperature.

12. It seems to be detrimental to the crystallization and recrystallization of the product to postpone the evaporation of the reaction mixture, probably because the product becomes contaminated with sulfur if the reduced reaction mixture is allowed to stand.

13. Sometimes difficulty is encountered in starting the crystallization, since the product may separate as a yellow oil. It is helpful to induce crystallization by rubbing the sides of the vessel with a stirring rod and seeding the solution with any crystals that form on the sides of the vessel during the evaporation.

14. The ligroin used was Skellysolve B.

15. About 30 ml. of warm absolute ethanol readily dissolves 8–9 g. of product. Addition of 15 ml. of water and cooling effect crystallization with about 90% recovery of product.

3. Methods and Merits of Preparation

Previously, diphenaldehyde has been made by the Ullman coupling of *o*-iodobenzaldehyde,^{5,6} by bromination of *o,o'*-bitolyl and hydrolysis of the resulting tetrabromo compound,⁷ and by lithium aluminum hydride reduction of the *N*-methylanilide of diphenic acid.⁸ These methods involve more steps and give poorer yields than ozonolysis of phenanthrene.

The present method is based on the earlier described ozonolysis of phenanthrene in methanol.⁹ The reduction of the peroxidic reaction mixture with trimethyl phosphite to give diphenaldehyde, isolated as the di-*p*-nitrophenylhydrazone, in quantitative yield has been described recently.¹⁰ The disadvantage of this method is that the dialdehyde cannot be isolated in the free state in high yield. Diphenaldehyde has also been obtained by sodium

iodide reduction of peroxidic products from ozonolysis of phenanthrene in solvents that do not react ² with the zwitterion intermediate.^{11,12} The yields are inferior to those obtained by the present method. The patent literature ¹³ reports an 81% yield of diphenaldehyde from ozonolysis of phenanthrene-anthracene mixtures in a *tert*-butyl alcohol-water mixture followed by hydrolysis. Whether this is satisfactory with phenanthrene alone or whether the product is pure was not stated.

¹ Department of Chemistry, University of Texas, Austin 12, Tex.

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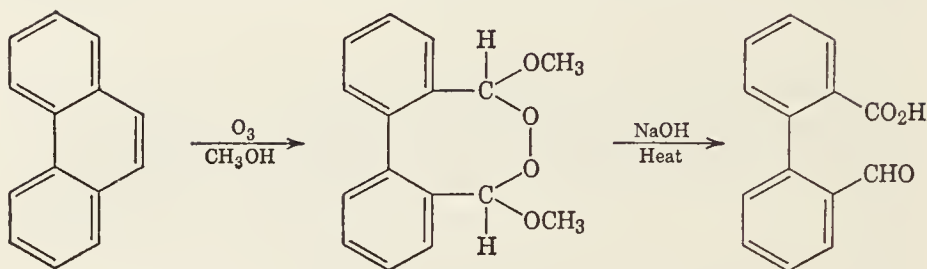
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DIPHENALDEHYDIC ACID

(2-Biphenylcarboxylic acid, 2'-formyl-)

Submitted by PHILIP S. BAILEY and RONALD E. ERICKSON.¹

Checked by CAROLE L. OLSON and JOHN D. ROBERTS.

1. Procedure

A. *3,8-Dimethoxy-4,5,6,7-dibenzo-1,2-dioxacyclooctane*. The ozonolysis of 10 g. (0.0562 mole) of phenanthrene in dry methanol is carried out as described in the diphenaldehyde preparation (p. 41). The reaction mixture is not reduced, however, but is acidified with 1–3 drops of concentrated hydrochloric acid (Note 1) and allowed to stand at room temperature for an hour and then in the refrigerator for several hours or overnight. Suction filtration yields 11.5–12.5 g. (75–82%) of crystals melting at 178–181°. Trituration with methyl ethyl ketone gives a 90–95% recovery of colorless crystals melting at 180–181° (Note 2).

B. *Diphenaldehydic acid*. A mixture of 10 g. (0.0368 mole) of 3,8-dimethoxy-4,5,6,7-dibenzo-1,2-dioxacyclooctane, 50 ml. of 10% sodium hydroxide solution, and 200 ml. of 95% ethyl alcohol is heated under reflux for 15 minutes, during which time the solid dissolves (Note 3). The solution is cooled, acidified with concentrated hydrochloric acid, and diluted to the cloud point with water. Crystallization is induced by rubbing the side of the vessel with a stirring rod (Note 4). More water is then added slowly until crystallization is complete. Filtration yields 6.7–7.3

g. (81–88%) of colorless to yellowish crystals melting at 130–132°. Recrystallization from 100 ml. of 1:1 methanol-water gives an 80–95% recovery of diphenaldehydic acid melting at 134–135° (Notes 5, 6, and 7).

2. Notes

1. The acid catalyzes formation of the dimethoxy compound from the initial ozonolysis products (see Note 6 of the diphenaldehyde preparation, p. 42). Compound I forms only slowly in the absence of the hydrochloric acid.

2. The trituration is carried out at room temperature, but the mixture is cooled before filtering. The product can be recrystallized from methyl ethyl ketone, but this requires large volumes of the solvent and is unnecessary.

3. After solution has occurred, 1 ml. of the solution is acidified and tested with sodium or potassium iodide. If no iodine is released, the reaction is complete.

4. If the solution resists crystallization, it can be evaporated one-half or two-thirds of its volume and cooled further. The checkers found that, if product was allowed to oil out and solidify, the subsequent purification was rendered more difficult.

5. Often recrystallization is unnecessary since the first crystalline product melts at 134–135°. The yields then are 81–84%.

6. If sodium hydroxide is omitted in this preparation and the reaction mixture is refluxed until it no longer gives a positive peroxide test with iodide ion (Note 3) (about 2 hours), the product is the methyl ester of diphenaldehydic acid in 91–98% yield (m.p. 50–51°).²

7. If, in the reaction mixture described, twice the volume of 10% sodium hydroxide solution and 25 ml. of 30% hydrogen peroxide are employed and the reaction mixture is refluxed until it no longer gives a positive peroxide test with iodide ion (about 30 minutes to 1 hour), the product is diphenic acid (m.p. 220–223°) in 73–85% yield.

3. Methods and Merits of Preparation

The method here described is based on the reported ozonolysis of phenanthrene in methanol, followed by conversion of the initial ozonolysis product to diphenaldehyde (p. 41), diphenaldehydic acid, methyl diphenaldehydate (Note 6), and diphenic acid (Note 7).² Diphenaldehydic acid has previously been made in low yields by oxidative decomposition of the monohydrazide of diphenic acid.^{3,4} The presently described method is far superior, not only in yield, but also in simplicity.

Diphenic acid has been prepared by the reduction of diazotized anthranilic acid with cuprous ion,⁵ Ullman coupling of potassium *o*-bromobenzoate,⁶ and oxidation of phenanthrene or phenanthrenequinone with various oxidizing agents.⁷ The latter methods have been reviewed recently.⁷ The ozonolysis method has also been carried out in solvents⁸ that do not react with the zwitterion intermediate.⁹

Of the various routes to diphenic acid, the present method and the peracetic acid oxidation of phenanthrene⁷ seem to be the simplest. The yields are equally good.

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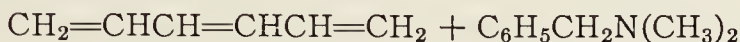
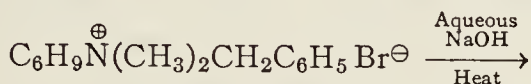
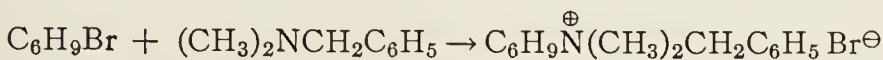
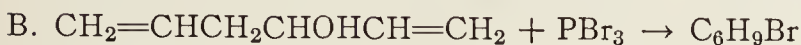
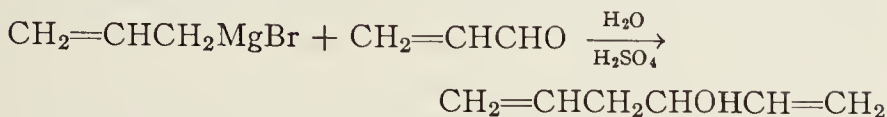
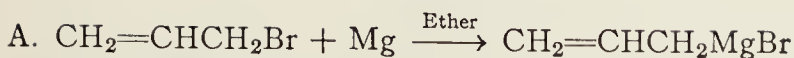
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1,3,5-HEXATRIENE



Submitted by JESSE C. H. HWA and HOMER SIMS.¹

Checked by VIRGIL BOEKELHEIDE and E. A. CARESS.

1. Procedure

A. *1,5-Hexadien-3-ol* (Note 1). In a 5-l. three-necked flask fitted with a stirrer, a dropping funnel and an ice-water condenser are placed 153.0 g. (6.28 g. atoms) of magnesium turnings, 360 ml. of anhydrous ether (Note 2), and a few crystals of iodine. A solution of 351.0 g. (2.90 moles) of allyl bromide (Note 3) in 2.6 l. of ether is added in small portions until the reaction begins, and then at such a rate as to maintain gentle refluxing of the ether. The addition requires about 3 hours, after which the reaction mixture is refluxed on a steam bath for an additional hour. Acrolein (Note 4) (104.0 g., 1.86 moles) is added during 2 hours, and this causes gentle refluxing. After an additional hour at room temperature the reaction mixture is poured slowly into 2 l. of ice water. The precipitate is dissolved by adding slowly a solution of 120 ml. of concentrated sulfuric acid (sp. gr. 1.84) in 400 ml. of water (Note 5). The organic layer is separated and the water layer extracted with three 200-ml. portions of ether. The combined oil and ether extracts are dried over 8–10 g. of anhydrous magnesium sulfate. After removal of the ether, the

residue is distilled through a 6-in. column packed with glass helices to yield 104–108 g. (57–59%, based on acrolein) of 1,5-hexadien-3-ol; b.p. 62–65/50 mm., n_D^{25} 1.4440.

B. *1,3,5-Hexatriene*. In a 500-ml., three-necked, round-bottomed flask fitted with a mechanical stirrer, a thermometer, and a graduated dropping funnel are placed 114 g. (0.42 mole) of phosphorus tribromide (Note 6) and 2 drops of 48% hydrobromic acid. As the contents of the flask are stirred and maintained at 10–15° by means of an ice-water bath, 98 g. (1.00 mole) of 1,5-hexadien-3-ol is added in the course of 1.5 to 1.75 hours. The mixture is allowed to stir at 10–15° for 40 minutes and then to stand at room temperature overnight. The flask is cooled in an ice-salt bath for 20 minutes, and the upper organic layer is decanted from the residue while still cold. The organic layer is successively washed with three 40-ml. portions each of ice water, 5% sodium bicarbonate, and water. The crude bromohexadiene weighs 147–153 g. (91–95%) (Note 7).

In an assembly similar to that used for the previous reaction, 90 g. (0.67 mole) of dimethylbenzylamine (Note 8), 0.13 g. of hydroquinone, and 500 ml. of water are stirred and heated at 50°. The crude bromohexadiene (107 g., 0.67 mole) is added in the course of 20–40 minutes, and stirring and heating are maintained at 50° for 2–2.5 more hours. The flask is then fitted for downward distillation, and the mixture is distilled at about 40–50° and 30 mm. until no more oil distills with the water. A total of 133–200 ml. of distillate is collected. This is discarded.

A solution of sodium hydroxide (106 g., 2.7 moles) in 535 ml. of water is placed in a 2-l. flask equipped with a sealed mechanical stirrer and an outlet arranged for downward distillation into an ice-cooled receiver. The aqueous solution of the quaternary bromide is added dropwise to the boiling solution of sodium hydroxide during a period of 2.5–4 hours (Note 9). The hexatriene and dimethylbenzylamine which form are distilled with the water. Distillation is continued for 10–15 minutes after the final addition of quaternary bromide solution. The clear upper layer of the distillate is separated, cooled to 5–10°, washed with three 170-ml. portions each of cold 2*N* hydrochloric acid and water, and dried over anhydrous sodium sulfate. The oil is then distilled,

a spinning-band column being used to give 32.0–34.0 g. (54–60%) of 1,3,5-hexatriene; b.p. 80–80.5°, n_D^{20} 1.5103–1.5119 (Note 10).

2. Notes

1. This method is essentially that of Butz, Butz, and Gaddis² except for modified charge ratios to increase the output per batch at some sacrifice in per cent yield.

2. Baker and Adamson, reagent grade.

3. Matheson, Coleman and Bell, b.p. 70–71°.

4. Shell Chemical Co., commercial grade, inhibited.

5. When the magnesium complex is dissolved, the solution may be decanted from the excess magnesium metal.

6. Dow Chemical Co., practical grade.

7. The moist crude bromohexadiene is quaternized in water without further purification. The submitters report that, if desired, the crude mixture may be dried over anhydrous calcium chloride and fractionally distilled through a 10-in. stainless-steel-packed column at reduced pressure. Crude bromohexadiene (220–230 g.) from 147 g. (1.50 moles) of 1,5-hexadiene-3-ol was found to give the fractions listed in Table I. The yield of the

TABLE I

Fraction	Wt., g.	B.P./mm.	n_D^{20}	Product
1	43.2	55–56°/34	1.4829	3-Bromo-1,5-hexadiene
2	31.7	57–72°/34	1.4923	Mixture of the 3- and 1-bromo isomers
3	70.7	72–73°/36	1.4981	1-Bromo-2,5-hexadiene
4	10.1	56–59°/18	1.4996	Mostly 1-bromo-2,5-hexadiene
5	19.2	64–103°/14	1.5196	—

total distillate is 174.9 g. of which fractions 1–4 amount to 155.7 g. (64.5%). The 1-bromo isomer has been reported in the literature,^{3,4} and the infrared spectrum suggests that fraction 1 is 3-bromo-1,5-hexadiene. Both isomers when treated separately in this procedure yield hexatriene.

8. The amine should be freshly distilled.

9. This time, although not critical, was chosen to prevent accumulation of unreacted quaternary base or of hexatriene in the reaction vessel.

10. The faintly yellow product obtained before distillation is quite pure. The infrared absorption spectra of the liquid before and after distillation are identical and have, in addition to all the bands shown in the published spectrum of Woods and Schwartzman,⁵ weak absorption bands, notably at 820, 989, 1187, and 1452 cm^{-1} . The differences between the two spectra are due to various ratios of *cis* and *trans* isomers in these hexatriene samples. The ratio of *cis*- to *trans*-1,3,5-hexatriene in this preparation is estimated at 3:7. This is based on studies using vapor-phase chromatography, ultraviolet absorption spectra, and refractive indices.⁶ The hexatriene is stored under nitrogen at -5° . Although no visible change is observed after 1 week of storage, the liquid is partially polymerized to the consistency of glycol after 3 weeks. Hexatriene can be removed from the thin syrup by distillation at 40 mm., and when redistilled at atmospheric pressure under nitrogen has b.p. 80.5° , n_D^{20} 1.5101. Its infrared absorption spectrum is then identical with that of freshly prepared hexatriene.

3. Methods and Merits of Preparation

1,3,5-Hexatriene has been prepared by many workers. The more successful methods are the catalytic pyrolyses (alumina, $260\text{--}325^{\circ}$) of 1,3-hexadien-5-ol^{5,7,8} and 2,4-hexadien-1-ol.⁹ Other methods which give hexatriene of questionable purity or involve less convenient laboratory methods are dehydration of 1,5-hexadien-3-ol by sodium bisulfate at 170° ,¹⁰ or by phthalic anhydride at $160\text{--}200^{\circ}$,² and by catalytic hydrogenation of divinylacetylene.¹¹ Additional methods are listed in footnote 5. The present procedure is a practical laboratory method of preparing pure hexatriene in satisfactory yields.

¹ Rohm and Haas Company, Philadelphia, Pa.

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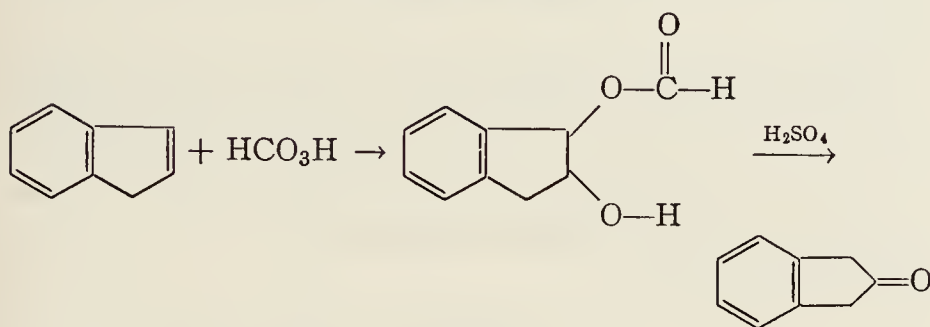
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2-INDANONE



Submitted by J. E. HORAN and R. W. SCHIESSLER.¹

Checked by WILLIAM E. PARHAM, WAYLAND E. NOLAND,
and ABDEL-MONEIM M. MAKKY.

1. Procedure

In a 2-l. three-necked flask fitted with stirrer, dropping funnel, and thermometer are placed 700 ml. of formic acid (88%) and 140 ml. of hydrogen peroxide (30%, 1.37 moles). While the temperature is kept at 35–40° (Note 1), 116.2 g. (117.3 ml., 1.00 mole) of indene (98%) (Note 2) is added dropwise, with stirring, over a period of 2 hours. An additional 100 ml. of formic acid is used to rinse the last of the indene from the dropping funnel into the reaction flask. The reaction solution is stirred at room temperature for 7 hours to ensure complete reaction (Note 3). The solution is transferred to a 2- or 3-l. Claisen flask, and the formic acid is removed under aspirator pressure (b.p. 35–40°/20–30 mm.), care being taken to maintain the boiler temperature below 60° (Note 4). The residue, after being cooled to room temperature, is a yellowish brown crystalline solid (Note 5), the color being due to contamination by a small amount of brownish oil.

In a 5-l. flask fitted with a long condenser (about 40 cm.) connected to an ice-cooled receiver is placed 2 l. of 7% (by volume) sulfuric acid. The solution is heated to boiling, and the crude monoformate of 1,2-indanediol is added. Steam is introduced and the mixture is steam distilled, while external heat is applied with a flame in order to maintain the boiler contents at a constant volume of 2 l. The steam distillation is carried out at the rate of about 1 l. per hour until 5–6 l. of distillate have been collected and the 2-indanone has stopped distilling (Note 6). The dark-brown oily residue becomes semisolid at room temperature.

The cold distillate is filtered with suction, and the white crystalline solid is sucked thoroughly dry on the filter (Note 7). The crystals are dried further in a vacuum desiccator (at about 1 mm.) at room temperature or below for about 12 hours. The melting point of the 2-indanone is 57–58° (Note 8). The yield is 90–107 g. (69–81%).

2. Notes

1. This is the best temperature at which to control the reaction. At higher temperatures, the reaction becomes too vigorous.

2. The indene ($n_D^{25.5}$ 1.5698, b.p. 74–76°/24 mm.) was obtained from Rütgerswerke, A. G., West Germany, through Terra Chemicals, Inc., 500 Fifth Avenue, New York 36, N. Y. It was faintly yellow, but was used without distillation, since distillation, although it removed the yellow color, did not change the refractive index. When Matheson, Coleman and Bell technical grade indene was used (redistilled, $n_D^{25.5}$ 1.5606, b.p. 177–179°), a 45% yield of 2-indanone was obtained.

3. The reaction mixture can be left overnight at this point with no adverse effect upon yield.

4. A higher temperature should be avoided at the start to prevent boilover, and later to reduce side reactions and eliminate danger from possible residual peroxides.

5. The reaction can be interrupted at this point and the formate ester stored for several weeks, if desired.

6. The rate of flow of cooling water through the condenser must be regulated so that the condenser does not become clogged

with 2-indanone. The end point of the distillation can be recognized by lack of turbidity in the condensate or of solidification in the condenser when cold water is passed rapidly through the condenser.

7. The steam distillate, with the 2-indanone under water, can be kept for as long as a week in the refrigerator. In the dry state, 2-indanone is unstable to air at room temperature but can be kept in a closed vessel for several days at room temperature and for longer periods (several weeks or more) in a refrigerator.

8. The ultraviolet spectrum in the 300–350 $m\mu$ region showed that less than 1% of 1-indanone was present. If the 2-indanone darkens on standing, it can be repurified by steam distillation or by crystallization from ethanol.

3. Methods of Preparation

2-Indanone was first prepared by distillation of the calcium salt of *o*-phenylenediacetic acid^{2,3} and, more recently, by the action of acetic anhydride on its potassium salt.⁴ It has been obtained by the dilute sulfuric acid-catalyzed hydrolysis and decarboxylation of 2-iminoindan-1-carboxylate⁵ and ethyl 2-indanone-1-carboxylate.⁶ 2-Indanone is commonly obtained by acid-catalyzed dehydration of an indene glycol,^{7,8} as illustrated in this preparation. Indene glycol has been obtained from indene via the bromohydrin.^{9–12} The most recent preparation of 2-indanone is by Curtius degradation of 2-indenecarboxylic acid.¹³

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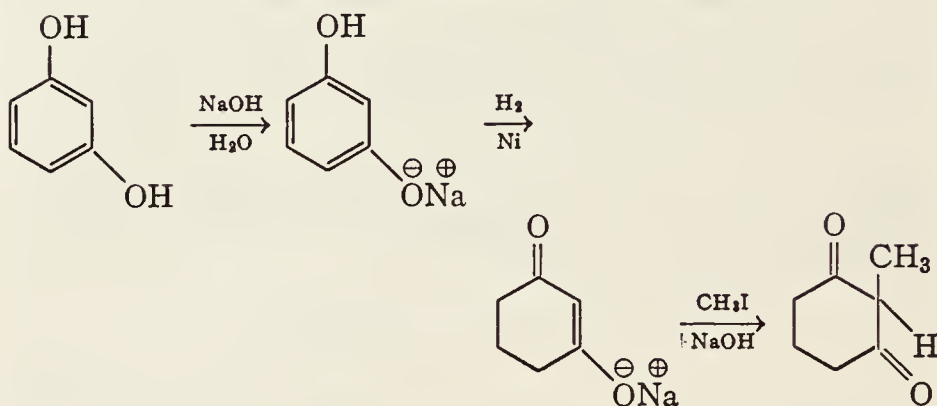
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2-METHYL-1,3-CYCLOHEXANEDIONE

(1,3-Cyclohexanedione, 2-methyl-)



Submitted by A. B. MEKLER, S. RAMACHANDRAN,
S. SWAMINATHAN, and MELVIN S. NEWMAN.¹
Checked by MAX TISHLER, A. J. ZAMBITO, and
W. B. WRIGHT.

1. Procedure

A freshly prepared solution of 96.0 g. (2.4 moles) of sodium hydroxide, 335 ml. of water, and 220.2 g. (2.0 moles) (Note 1) of resorcinol (Note 2) is placed in a 1.3-l. hydrogenation bomb together with 40.0 g. of finely powdered nickel catalyst (Note 3). The hydrogenation is carried out under an initial pressure of about 1900 lb. of hydrogen with agitation. The reaction is slightly exothermic, and gentle heating is applied to maintain a temperature of 45–50° (Note 4). The hydrogenation is continued until about a 10% excess of the theoretical amount of hydrogen (2.0 moles) has been absorbed (Note 5). At this point, the agitation is stopped, and the bomb is cooled to room temperature. The reaction mixture is poured into a 1-l. beaker, and the catalyst is removed by filtration with the aid of three 50-ml. portions of water for the combined operations. The filtrate and washings are transferred to a 2-l. round-bottomed flask and treated with

33.5 ml. of concentrated hydrochloric acid (for partial neutralization), 145 ml. of dioxane, and 335 g. (2.4 moles) of methyl iodide (Note 6). The reaction mixture is refluxed for a total of 12–14 hours. After 7 or 8 hours, an additional 33.5 g. (0.24 mole) of methyl iodide is added. The system is cooled several hours in an ice bath, and the 2-methyl-1,3-cyclohexanedione which crystallizes is collected by filtration (Note 7), washed with four 200-ml. portions of cold water (Note 8), and then dried in an oven at 110°. The initial crop of dione, m.p. 206–208° dec., weighs 138–142 g. (54–56%). The mother liquors are concentrated under reduced pressure to one-half of their original volume and are then cooled in an ice-salt bath to yield an additional 7–11 g. (3–5%) of slightly yellow dione which melts at 200–204° dec.

The 2-methyl-1,3-cyclohexanedione thus obtained (Note 9) can be purified by recrystallization from 95% ethanol, using about 20 ml. of ethanol for each 5 g. of product to give colorless crystals, m.p. 208–210° dec., with only minor loss of material.

2. Notes

1. The submitters have carried out runs with as much as 990 g. (9.0 moles) of resorcinol.

2. Both Merck resorcinol U.S.P. powder and resorcinol of practical grade give satisfactory results.

3. Many different nickel catalysts have been used: e.g., Grade 0140T1/8 Harshaw Chemical Co., Cleveland 6, Ohio; reduced Universal Oil Products hydrogenation catalyst pellets which are pulverized just before use; and Raney nickel catalyst W-2. Before using the Raney nickel, care must be taken to free it of aluminum by careful washing with 5% sodium hydroxide solution, followed by thorough rinsing with distilled water (private communication from Dr. Richard Weiss, van Ameringen-Haebler, Inc., New York 19, N. Y.). The checkers prepared Raney nickel catalyst W-2 according to the procedure in *Org. Syntheses*, Coll. Vol. 3, 181 (1955).

4. The temperature should not exceed 50°; at higher temperatures complex condensation products result.

5. The length of time required for the hydrogenation varies with the size of the run and the activity of the catalyst. For a 9-mole run the hydrogenation usually proceeds for 10–12 hours before external heating is needed to bring the temperature into the 45–50° range. The system is periodically recharged with hydrogen to maintain a pressure of about 1800 lb. Reduction is continued until a total of 9.0 moles of hydrogen has been absorbed. Absorption of the calculated amount of hydrogen serves as the criterion for stopping the hydrogenation. For the 2.0-mole run described, 4–5 hours are needed.

6. The conversion of resorcinol to 2-methyl-1,3-cyclohexanedione can be effected by first isolating the dihydroresorcinol ² and subjecting it to the methylation reaction. However, this procedure is more laborious and the yield is no better.

7. The checkers found that filtration through a coarse sintered-glass funnel is rapid and better-quality product is obtained. When a medium-porosity sintered-glass funnel or Büchner funnel is used, the filtration is exceedingly slow and may even stop owing to a small amount of gelatinous impurity which is present.

8. If all the sodium iodide is not removed by the washings with water, the product tends to become yellow.

9. This product is sufficiently pure for use in conversion to 1,6-dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene.^{3,4}

3. Methods of Preparation

2-Methyl-1,3-cyclohexanedione has been prepared by cyclization of ethyl 5-oxoheptanoate ⁵ and methyl 5-oxoheptanoate ³ with sodium ethoxide and sodium methoxide, respectively, and by methylation of dihydroresorcinol ² employing sodium methoxide in methanol,^{3,6} potassium hydroxide in aqueous methanol,⁷ potassium methoxide in methanol,⁸ potassium hydroxide in aqueous acetone,⁹ potassium carbonate in aqueous acetone,⁴ or sodium ethoxide in ethanol.¹⁰ The present method is essentially that of Stetter,⁷ except that the unnecessary isolation of the intermediary dihydroresorcinol is omitted, and this greatly enhances the ease of preparation.

4. Merits of Preparation

2-Methyl-1,3-cyclohexanedione has been used as starting material for the syntheses of several polycyclic compounds for projected syntheses of steroids and terpenoids.¹¹⁻¹³ It has also been used to prepare 1,6-diketo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene.^{3, 4, 14, 15}

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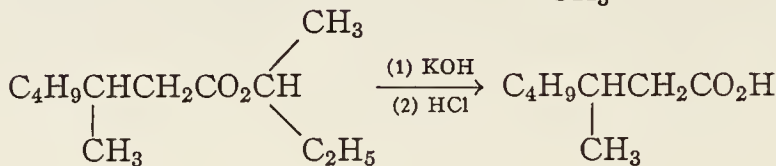
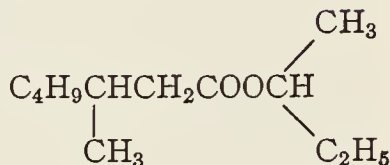
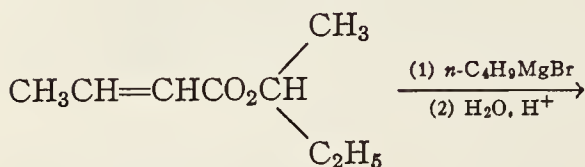
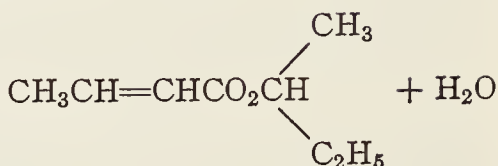
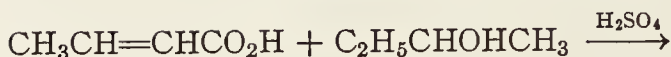
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3-METHYLHEPTANOIC ACID

(Heptanoic acid, 3-methyl-)

Submitted by JON MUNCH-PETERSEN.¹

Checked by MELVIN S. NEWMAN and DONALD E. HARSH.

1. Procedure

A. *sec*-Butyl crotonate. In a 2-l. round-bottomed flask are placed 258 g. (3 moles) of crotonic acid (Note 1), 370 g. (5 moles) of *sec*-butyl alcohol in which has been dissolved 6–7 ml. of concentrated sulfuric acid, and 300 ml. of benzene. A few boiling chips are added, and the flask is fitted with a suitable water separator (Note 2) in the top of which is placed a reflux condenser. The mixture is heated under reflux for about 12 hours or until no further separation of aqueous phase occurs. About 65 ml. of water is collected. The cooled reaction mixture is diluted with 200 ml. of ether, washed with 10% sodium carbonate solution

until neutral to litmus, washed with saturated sodium chloride solution, and finally dried over magnesium sulfate. The solvent is distilled, and the ester is fractionated under reduced pressure through a small column. The yield of *sec*-butyl crotonate, b.p. 74–75°/30 mm. or 83–84°/45 mm., n_D^{25} 1.4261, is 360–390 g. (85–90%) (Note 3).

B. *3-Methylheptanoic acid*. In a 2-l. three-necked flask fitted with a mercury-sealed stirrer, a reflux condenser carrying a calcium chloride tube, and a dropping funnel are placed 25.0 g. (1.04 g. atoms) of magnesium turnings. The flask is heated to about 100° for a few minutes and then cooled to room temperature. A solution of 178 g. (1.30 moles) of *n*-butyl bromide in 300 ml. of dry ether is prepared; and of this solution about 10 ml., together with 30 ml. of dry ether, is run into the flask. The reaction is started by heating to reflux for a few seconds, the stirrer is started, and the remainder of the bromide solution is added at such a rate as to maintain constant reflux (about 1 hour).

After the addition has been completed, the solution is heated under reflux for 10–15 minutes. The flask is now surrounded by an ice and water bath, and stirring is continued for 15 minutes (Note 4). From a graduated dropping funnel, a solution of 56.8 g. (0.4 mole) of *sec*-butyl crotonate (Note 5) in 400 ml. of dry ether is then added dropwise during a period of about 3 hours (Note 6) while the reaction mixture is effectively stirred and cooled in the ice bath. After the addition of the ester solution is complete, the reaction mixture is stirred in the ice bath for an additional 15 minutes. The ice bath is then removed, and stirring of the grayish brown solution is continued at room temperature for 1 hour.

In a 3-l. Erlenmeyer flask are placed about 500 g. of crushed ice, 110 ml. (1.3 equivalents) of concentrated hydrochloric acid, and 100 ml. of ether. This mixture is vigorously swirled and shaken while the Grignard reaction mixture is cautiously added in small portions. More ice is added to the Erlenmeyer flask as required to keep the temperature near 0°. The resulting mixture is poured into a separatory funnel and shaken thoroughly. The water layer is separated and extracted three times with 100 ml. of ether. The combined ether solutions are washed with 100 ml. of sat-

urated sodium bicarbonate solution, and then with 100 ml. of water. The solution is dried over anhydrous magnesium sulfate, and the ether distilled on a water bath. The residue is fractionated at reduced pressure through a modified Claisen flask to yield 54–62 g. (68–78%) (Note 4) of *sec*-butyl 3-methylheptanoate, b.p. 92–93°/9 mm., n_D^{25} 1.4190.

A solution of 40 g. (0.2 mole) of *sec*-butyl 3-methylheptanoate in 100 ml. of ethanol containing 18.5 g. (0.3 mole) of potassium hydroxide and 20 ml. of water is heated under reflux for 30 minutes (Notes 7 and 8). The cooled solution is diluted with 200 ml. of water and acidified by the addition of 60 ml. of concentrated hydrochloric acid. The organic acid is extracted with three 100-ml. portions of 1:1 benzene-ether, and the combined benzene-ether extracts are washed with 50 ml. of saturated sodium chloride solution. The resulting solution is filtered by gravity through a bed of anhydrous magnesium sulfate. After removal of solvents by distillation, 26–27 g. (90–94%) of 3-methylheptanoic acid, b.p. 116–117°/10 mm., n_D^{25} 1.4242, is obtained by distillation in a modified Claisen flask (Note 9).

2. Notes

1. Eastman Organic Chemicals practical grade of crotonic acid (containing 10% water) was used by the checkers without further purification.

2. The water separator preferred by the submitter is that described by Wideqvist,² but any continuous water separator which will return the benzene to the reaction mixture may be used, e.g., the modified Dean-Stark water separator.³

3. By essentially the same procedure the submitter has prepared the following *sec*-butyl esters: *sec*-butyl acrylate, b.p. 127–129°, n_D^{20} 1.4158; *sec*-butyl methacrylate, b.p. 59–62°/34 mm., n_D^{25} 1.4161; *sec*-butyl tiglate, b.p. 84.5°/27 mm., n_D^{25} 1.4332; *sec*-butyl β,β -dimethylacrylate, b.p. 68–70°/13 mm., n_D^{25} 1.4379; *sec*-butyl cinnamate, b.p. 122°/2 mm., n_D^{25} 1.5382. With *sec*-butyl acrylate and methacrylate, 2–3% of hydroquinone should be added to the reaction mixtures and 0.1% of hydroquinone to the esters if stored at room temperature.

4. Recent investigations⁴ by the submitter have shown that the yield of *sec*-butyl 3-methylheptanoate is improved to 80–85% if 1.4 g. (1.4 mole% with respect to the Grignard reagent) of cuprous chloride (commercial grade, analytically pure) is added in seven portions during the course of the addition of the ester.

5. Ethyl crotonate may be used with the same yield (70%) of addition product if cuprous chloride is present during the addition⁵ (cf. Note 4). Methyl crotonate under these conditions yields methyl α,γ -di-(2-hexyl)-acetoacetate [methyl 2-(2'-hexyl)-3-keto-5-methylnonanoate], b.p. 135°/2.5 mm., n_D^{25} 1.4419, in 67% yield.⁶

6. The large excess of Grignard reagent, the dilution of the ester, and the slow addition are essential features of the procedure. If these conditions are not fulfilled the yields drop considerably, and a greater amount of high-boiling residue, di-*sec*-butyl α -(2-hexyl)- β -methylglutarate, b.p. 145°/1.5 mm., n_D^{25} 1.4400, is formed.⁶ When the reaction is run on a 0.2-mole scale the addition time of the ester may be reduced to 1.5 hours.

7. In the case of the analogous products obtained by the addition reactions with *sec*-butyl tiglate (cf. Note 9) considerably more drastic conditions are necessary in order to secure complete saponification. The submitter generally employs reflux for 6–8 hours with 35 g. (0.6 mole) of potassium hydroxide dissolved in 250 ml. of 95% ethanol.

8. An alternative procedure is used by the submitter from this point to the final distillation of solvent and ester: The condenser is then set for downward distillation, and about 40 ml. of alcohol is distilled. Then 100 ml. of water is added, and an additional 100 ml. of alcohol and water is distilled. The cooled residue is diluted with 200 ml. of water and the solution freed of insoluble organic material by washing three times with 50 ml. of ether. After acidification with 40 ml. of concentrated hydrochloric acid, the organic layer is extracted with three 50-ml. portions of ether. The combined ether extracts are washed with water and dried over anhydrous magnesium sulfate.

9. The submitter has, by either cuprous chloride-catalyzed or uncatalyzed reactions, prepared a variety of 3-methyl-substituted fatty acids from the adducts of *sec*-butyl crotonate and other

Grignard reagents.⁴⁻⁹ The uncatalyzed reaction has also been used with *sec*-butyl tiglate to obtain 2,3-dimethyl-substituted fatty acids.⁷

Methods of Preparation

3-Methylheptanoic acid has been prepared by mixed electrolysis of β -methylglutaric acid monomethyl ester and butyric acid, followed by saponification of the methyl ester,¹⁰ and by the malonic ester synthesis from 2-bromohexane.¹¹ The present method⁷ has the advantage of avoiding the use of secondary bromides, which are often difficult to secure entirely pure.¹²

4. Merits of Procedure

The reactions here described are of considerable general utility for the preparation of a variety of fatty acids from the addition products of Grignard reagents and α,β -unsaturated esters.⁴⁻⁹

¹ Department of Organic Chemistry, Polyteknisk Laereanstalt, Copenhagen, Denmark.

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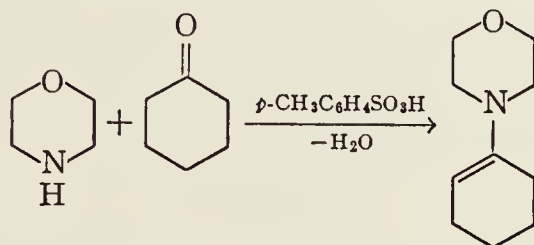
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1-MORPHOLINO-1-CYCLOHEXENE

[Morpholine, 4-(1-cyclohexenyl)-]

Submitted by S. HÜNIG, E. LÜCKE, and W. BRENNINGER.¹

Checked by B. C. MCKUSICK and F. E. MUMFORD.

1. Procedure

A solution of 147 g. (1.50 moles) of cyclohexanone, 157 g. (1.80 moles) of morpholine (Note 1), and 1.5 g. of *p*-toluenesulfonic acid in 300 ml. of toluene is heated to boiling in a 1-l. round-bottomed flask to which is attached a water separator² under a reflux condenser. The separation of water begins at once and ceases after 4 or 5 hours. An indented Claisen stillhead is attached to the flask, and the reaction mixture is distilled. Most of the toluene is removed at atmospheric pressure. 1-Morpholino-1-cyclohexene is collected as a colorless liquid at 118–120°/10 mm.; n_D^{25} 1.5122–1.5129 (Note 2). It weighs 180–200 g. (72–80%).

2. Notes

1. An excess of morpholine is required because the water that separates during the reaction always contains a considerable amount of it in solution.

2. 1-Morpholino-1-cyclohexene is very easily hydrolyzed. Accordingly one must be careful to keep moisture out. On long standing in a refrigerator, the compound generally becomes somewhat yellowish, but this does not affect its usefulness in subsequent reactions.

3. Methods of Preparation

The procedure is that of Hünig, Benzing and Lücke.³ It is based on earlier work on the preparation of enamines.^{4,5}

4. Merits of Preparation

This is a general method of preparing enamines from a secondary aliphatic amine and cyclohexanone or cyclopentanone. Acylation of such enamines is the first step in a general procedure for increasing the chain length of a carboxylic acid by 5 or 6 carbon atoms and of a dicarboxylic acid by 10 or 12 carbon atoms.⁶ Alkylation of enamines of cyclohexanones by alkyl halides^{5,7} or electrophilic olefins,⁸ followed by hydrolysis, is a good route to α -monoalkylcyclohexanones.

¹ University of Marburg, Marburg, Germany.

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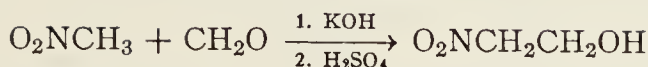
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2-NITROETHANOL

(Ethanol, 2-nitro-)

Submitted by WAYLAND E. NOLAND.¹

Checked by MELVIN S. NEWMAN and SURJAN S. RAWALAY.

1. Procedure

In a 5-l., three-necked, round-bottomed flask fitted with a 30-ml. dropping funnel, mechanical stirrer, and thermometer extending down into the liquid is placed a suspension of paraformaldehyde (trioxymethylene, 125 g., 4.16 moles) in freshly distilled (Note 1) nitromethane (2.5 l., 46.6 moles). The suspension is stirred vigorously, and 3*N* methanolic potassium hydroxide solution is added dropwise from the dropping funnel until, at an apparent pH of 6–8, but closer to pH 8 (pH paper), the paraformaldehyde begins to dissolve and the suspension assumes a clearer appearance. About 10 ml. of the alkaline solution is required, and the addition takes about 10 minutes. About 15–20 minutes after addition of the alkaline solution is complete, the paraformaldehyde dissolves completely. Shortly thereafter, the solution temperature reaches a maximum of 13–14 degrees above room temperature and then slowly drops. Stirring is continued 1 hour after addition of the alkaline solution is complete.

Stirring is continued while the added alkali is *completely* neutralized by adding concentrated (36*N*) sulfuric acid (1 ml.) dropwise from a medicine dropper over a period of about 3 minutes until an apparent pH of about 4 is reached (Note 2). The solution is then stirred for an hour, during which time the pH should not change (Note 3).

The precipitated potassium sulfate is filtered by passing the solution through a 12-cm. Büchner funnel. The light-yellow or yellowish green filtrate is transferred to a 5-l., one-necked, round-

bottomed flask fitted with a Claisen head containing a capillary ebulliator tube and a thermometer, and connected to a water-cooled condenser. The condenser is connected through a vacuum adapter to a 3-l., one-necked, round-bottomed flask, cooled in ice, to act as a receiver. About 2.3 l. of pure, unchanged nitromethane is removed by distillation at aspirator pressure and a water-bath temperature of 40–50°. The distillation takes about 6–7 hours.

The golden-yellow residue (315–365 g.) is transferred to a 1-l., one-necked, round-bottomed flask containing an equal weight of diphenyl ether (Note 4). The flask is fitted with a Claisen head containing a capillary ebulliator tube and a thermometer, and connected to a water-cooled condenser. The condenser is connected to a 3- or 4-port fraction cutter fitted with 100–500 ml., one-necked, round-bottomed flasks, at least one of which is 500 ml. or larger to accommodate the main fraction (Note 5). The mixture is distilled under the vacuum of a good pump. The fore-run, b.p. 29–33° at about 0.10 mm., consisting of nitromethane (about 56 ml.), can be distilled at a water-bath temperature of 32–79° and usually passes directly into the Dry Ice trap protecting the vacuum pump. The temperature then rises as 2-nitroethanol and diphenyl ether codistil. The main fraction, a two-phase distillate initially richer in 2-nitroethanol than diphenyl ether, gradually changes in composition until the proportion of 2-nitroethanol becomes negligible. The main fraction of 410–425 g., b.p. 54–57° at about 0.10 mm. (or 64–66° at about 0.4 mm.), collects at a water-bath temperature of 79–88°. Care should be taken to prevent clogging of the condenser or fraction cutter with solid diphenyl ether (m.p. 27°). The distillation is continued until the proportion of 2-nitroethanol (lower layer) observed in the distillate becomes negligible, and the temperature suddenly starts to rise. At this point heating is stopped, *but the residue is cooled to room temperature or below before the vacuum is broken* (Note 6).

The two-phase main fraction of the distillate is placed in a 500-ml. separatory funnel and the lower layer of crude 2-nitroethanol (185–200 g., 146–158 ml., n_D^{25} 1.4493–1.4513, containing about 92–94 mole % 2-nitroethanol) is drawn off. The 2-nitroethanol is then extracted in a 500-ml. separatory funnel with an

equal volume of light petroleum ether (b.p. 60–68°, such as Skellysolve B) or hexane, and the colorless lower layer of 2-nitroethanol (174–188 g., 46–49%, n_D^{25} 1.4432–1.4433, containing about 98 mole % 2-nitroethanol) is drawn off (Notes 7 and 8). The product turns light yellow after standing for a day or more.

2. Notes

1. Commercial nitromethane is sometimes quite acidic, and much more methanolic potassium hydroxide is required to initiate the reaction when such material is used. For safety, the nitromethane should be distilled at aspirator pressure instead of atmospheric pressure.

2. Sulfuric acid *must* be used in an amount slightly *more* than enough exactly to neutralize the alkali, and not just sufficient to make the reaction acidic. Otherwise, the metal salts of nitromethane can form explosive fulminates upon heating.

3. This is a suitable point at which to interrupt the experiment overnight.

4. 2-Nitroethanol prepared by the formaldehyde-nitromethane method should not be distilled without use of diphenyl ether as a heat-dispersing agent. The residue, consisting of di- and tri-condensation products of formaldehyde with nitromethane, when hot and concentrated, and particularly when the vacuum is broken and air is let in on the hot distillation residue, is very likely to undergo a flash detonation, or at least a fume-off which may proceed with explosive violence. Use of diphenyl ether is a wise safety precaution in the distillation of 2-nitroethanol made by other methods as well.

5. If a fraction cutter is not used, the residue should be cooled to room temperature each time before the vacuum is broken.

6. The large amount of diphenyl ether (80–125 g.) left as the upper layer in the distilling flask has served the useful purpose, by its mass and volatility, of preventing superheating of the residue and subsequent violent decomposition, as described in Note 4.

7. This procedure has been carried out 30 times by students in the advanced organic laboratory course at the University of

Minnesota. The extreme ranges of yields obtained were 32–52%, and the median yield was 46%.

8. The 2-nitroethanol obtained by this procedure is quite satisfactory for synthetic purposes, such as the preparation of nitroethylene. The small amount of light petroleum ether dissolved in the 2-nitroethanol can easily be removed under reduced pressure. Most of the remaining diphenyl ether can be removed by one redistillation under vacuum, since the fore-run is relatively rich in diphenyl ether. The main fraction has n_D^{25} 1.4425–1.4431. Although vacuum redistillation of 2-nitroethanol which has been freed by the present procedure from higher condensation products of formaldehyde with nitromethane is relatively safe, it is recommended that the procedure be carried out behind a safety shield or a barricade.

3. Methods of Preparation

The present procedure is that of Controulis, Rebstock, and Crooks,² modified to include the diphenyl ether purification method of Roy.³ 2-Nitroethanol has been prepared by condensation of formaldehyde (usually employed in the solid form as paraformaldehyde) with a large excess of nitromethane in the presence of an alkali catalyst,^{2,4-6} as illustrated by the present procedure, or in the presence of a strongly basic ion-exchange resin.⁷ Dimethoxymethane has also served as a source of formaldehyde in a reaction catalyzed by a mixture of acidic and basic ion-exchange resins.⁸ 2-Nitroethanol has also been prepared by the action of silver nitrite on 2-iodoethanol (ethylene iodohydrin);⁹⁻¹² by selective catalytic hydrogenation over 5% palladium on barium sulfate in pyridine solution of halogenated derivatives, including 2-chloro-2-nitroethanol, 2,2-dichloro-2-nitroethanol, and 2-bromo-2-nitroethanol;¹³ by the action of fuming nitric acid on ethylene;¹⁴ and by the action of dinitrogen tetroxide on ethylene in the presence of oxygen¹⁵⁻¹⁹ or nitric oxide,²⁰ or in carbon tetrachloride solution.²¹ The preparation of 2-nitroethanol from ethylene oxide by the action of aqueous solutions of barium,²² calcium,²² magnesium,²³ or zinc²² nitrite, or by the action of sodium nitrite and carbon dioxide,²⁴ has also been reported. The submitter has

been unable to prepare 2-nitroethanol from ethylene oxide using the procedures described for barium⁶ or sodium nitrite; his observation with respect to barium nitrite has been confirmed in another laboratory.²⁵ The action of dinitrogen tetroxide on ethylene oxide in chloroform solution has been reported to yield 2-nitroethyl nitrate, from which 2-nitroethanol could be obtained by alkaline saponification.²⁶ This report has since been refuted with the finding that the initial product is the mononitrite mononitrate ester of ethylene glycol, which saponifies to ethylene glycol mononitrate and diethylene glycol mononitrate.²⁷

4. Merits of Preparation

The present procedure has the advantage of using inexpensive, commercially available starting materials, combined with an apparently safe method of isolating the product. 2-Nitroethanol is particularly valuable as a synthetic intermediate for the preparation of nitroethylene. Nitroethylene is conveniently prepared by heating 2-nitroethanol with phthalic anhydride and allowing the nitroethylene to distil under reduced pressure.^{28,29}

¹ School of Chemistry, University of Minnesota, Minneapolis 14, Minn.

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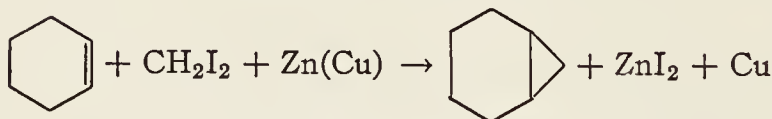
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NORCARANE

(Bicyclo[4.1.0]heptane)



Submitted by R. D. SMITH and H. E. SIMMONS.¹

Checked by WILLIAM E. PARHAM and M. D. BHAVSAR.

1. Procedure

A. *Zinc-copper couple.* In a 500-ml. Erlenmeyer flask fitted with a magnetic stirrer are placed 49.2 g. (0.75 g. atom) of zinc powder (Note 1) and 40 ml. of 3% hydrochloric acid. The mixture is stirred rapidly for 1 minute, then the supernatant liquid is decanted. In a similar manner, the zinc powder is washed successively with three additional 40-ml. portions of 3% hydro-

chloric acid, five 100-ml. portions of distilled water, two 75-ml. portions of 2% aqueous copper sulfate solution, five 100-ml. portions of distilled water, four 100-ml. portions of absolute ethanol, and five 100-ml. portions of absolute ether (Note 2). The couple is finally transferred to a Büchner funnel, washed with additional anhydrous ether, covered tightly with a rubber dam, and suction-dried until it reaches room temperature. The zinc-copper couple is stored overnight in a vacuum desiccator over phosphorus pentoxide and is then ready for use in the preparation of norcarane (Note 3).

B. *Norcarane*. In a 500-ml. round-bottomed flask fitted with a magnetic stirrer and a reflux condenser protected by a drying tube filled with Drierite are placed 46.8 g. (0.72 g. atom) of zinc-copper couple and 250 ml. of anhydrous ether. A crystal of iodine is added, and the mixture is stirred until the brown color has disappeared (Note 4). A mixture of 53.3 g. (0.65 mole) of cyclohexene and 190 g. (0.71 mole) of methylene iodide is added in one portion (Note 5). The reaction mixture is then heated under gentle reflux with stirring. After 30–45 minutes, a mildly exothermic reaction occurs which may require cessation of external heating. After the exothermic reaction has subsided (approximately 30 minutes), the mixture is stirred under reflux for 15 hours. At the end of this time, most of the gray couple has been converted to finely divided copper. The ether solution is decanted (Note 6) from the copper and unreacted couple, which are then washed with two 30-ml. portions of ether. The washes are combined with the bulk of the solution and shaken with two 100-ml. portions of saturated ammonium chloride solution (Note 7), 100 ml. of saturated sodium bicarbonate solution, and 100 ml. of water. The ether solution is dried over anhydrous magnesium sulfate and filtered. The ether is distilled through a 20 x 2-cm. column packed with glass helices. The residue is distilled through a 45-cm. spinning-band column² to give 35–36 g. (56–58%) of norcarane, b.p. 116–117°, n_D^{25} 1.4546 (Note 8).

2. Notes

1. Mallinckrodt A. R. zinc dust was found satisfactory for this preparation. The checkers used Merck zinc dust but found it necessary to start with 51 g. of zinc in order to obtain sufficient couple for the next step.

2. The washings with hydrochloric acid should be done rapidly to avoid adsorption of bubbles of hydrogen on the zinc which make subsequent washings more difficult. The use of a magnetic stirrer greatly facilitates the washings. The absolute ethanol and absolute ether washings are decanted directly on a Büchner funnel to prevent loss of the couple.

3. This method of preparing zinc-copper couple is essentially that of Shank and Shechter.³ An equally active couple can be prepared by reduction of cupric oxide in the presence of zinc powder.⁴ Mallinckrodt A. R. wire-form cupric oxide (30 g.) is ground to a powder in a mortar and mixed with 240 g. of Mallinckrodt A. R. zinc dust. The mixture is placed in a Vycor combustion boat lined with copper foil, and a thermocouple is imbedded in the powder. The boat is placed in a Vycor tube heated by a muffle furnace. A mixed gas (hydrogen, 65 l. per hour; nitrogen, 25 l. per hour) is passed through the tube while the temperature is raised to 500° during 4 hours. The mixture is kept at 500° for 30 minutes, and the tube is then allowed to cool to room temperature in a hydrogen atmosphere. The zinc-copper couple is obtained as dark gray lumps, which are ground to a fine powder in a mortar before use. In some instances, there is also found in the mixture a small amount of material which has apparently melted and agglomerated during heating. This shiny, metallic material is easily separated from the powdered couple and is not used in the preparation of norcarane.

4. The addition of iodine appears to promote the subsequent reaction of the zinc-copper couple with methylene iodide.

5. Commercial cyclohexene (Eastman Kodak) was distilled and passed over a column of activated alumina just before use. Methylene iodide (Matheson, Coleman and Bell) was distilled under reduced pressure, b.p. 50–51°/7 mm., and was stored in a brown bottle over iron wire.

6. The checkers filtered the solution because the finely divided copper and unreacted couple did not settle completely.

7. Care must be taken when adding the ammonium chloride solution to the ether solution since considerable heat is generated.

8. About 10–12 g. of cyclohexene, b.p. 82–84°, is recovered. The intermediate fraction, b.p. 84–116°, amounts to 1.5–2.5 g., and 10–12 g. of a dark residue remains in the still pot.

3. Methods of Preparation

Norcarane has been prepared by the reduction of 7,7-dichloronorcarane with sodium and alcohol,⁵ and by the light-catalyzed reaction of diazomethane with cyclohexene.⁵ The reaction of cyclohexene with methylene iodide and zinc-copper couple represents the most convenient preparation of norcarane which is of high purity.

4. Merits of Preparation

This method is generally applicable to the stereospecific synthesis of cyclopropane derivatives from a large variety of substituted olefins.⁴

¹ Contribution No. 622 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Co., Wilmington, Del.

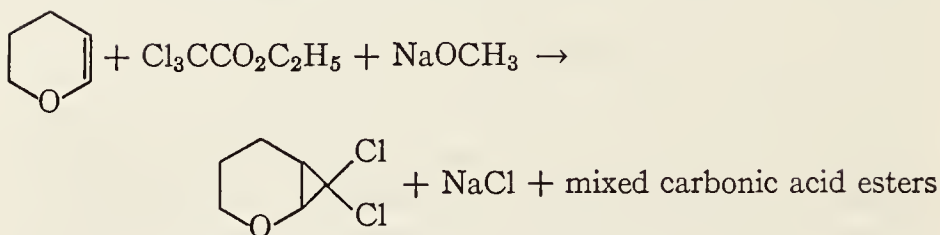
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2-OXA-7,7-DICHLORONORCARANE
(7,7-Dichloro-2-oxabicyclo[4.1.0]heptane)



Submitted by WILLIAM E. PARHAM, EDWARD E. SCHWEIZER, and
 SIGMUND A. MIERZWA, JR.¹

Checked by WILLIAM G. DAUBEN and RICHARD ELLIS.

1. Procedure

In a 1-l. three-necked flask (Note 1) is placed 50 g. (0.92 mole) of sodium methoxide (Notes 2 and 3). The flask is temporarily stoppered and then fitted with a nitrogen inlet tube, a sealed stirrer, and a 250-ml. pressure-equalized dropping funnel carrying a calcium chloride tube.

The dropping funnel is removed, and 67.4 g. (0.8 mole) of dihydropyran (Note 4) and 600 ml. of dry, olefin-free pentane (Note 5) are added successively. The light-yellow solution is stirred for 15 minutes in an ice-water bath, and then 164.8 g. (0.86 mole) of ethyl trichloroacetate (Note 6) is added from the dropping funnel over a period of 3–4 minutes. The dropping funnel is removed and replaced by a calcium chloride tube.

The reaction mixture is stirred for 6 hours (Note 7) at the ice-bath temperature and then is allowed to warm to room temperature overnight while the stirring is continued. During this period the color of the mixture changes from yellow-orange to brown.

Water (200 ml.) is added, the mixture is transferred to a 2-l. separatory funnel and shaken. The layers are separated and the

aqueous layer is extracted twice with 100-ml. portions of petroleum ether (b.p. 60–68°). The organic layers are combined and dried over anhydrous magnesium sulfate.

The solvent is removed at a maximum water-bath temperature of 60° and a minimum pressure of 30 mm. (Note 8). The residual liquid is distilled through a 25-cm. Vigreux column, and the fraction boiling at 74–76/8 mm. is collected (Note 9). The yield of 2-oxa-7,7-dichloronorcarane is 91–100 g. (68–75%), n_D^{25} 1.4974–1.4983.

2. Notes

1. All the glassware used is dried in an oven at 120°. The reaction vessel is arranged so that all the steps prior to hydrolysis are carried out under a constant positive pressure of dry nitrogen.

2. The sodium methoxide was obtained from Matheson, Coleman and Bell Co. The submitters carried out all operations with this reagent in a dry-box under a stream of dry nitrogen. Sodium ethoxide and potassium *tert*-butoxide have been successfully substituted for sodium methoxide;² the choice of sodium methoxide is here principally one of convenience. With other olefins, the choice of alkoxide depends upon the boiling points of the dichlorocarbene adduct and the corresponding dialkyl carbonates.

3. The checkers did not use a dry-box but simply rapidly weighed the sodium methoxide on a balance which was constantly swept with a stream of dry nitrogen from a large inverted funnel and then transferred the solid directly to the reaction flask.

4. The dihydropyran (Matheson) is dried over sodium carbonate and distilled once prior to use.

5. Technical grade pentane (Eastman Kodak) is freed of olefins by five successive washes each with 100 ml. of concentrated sulfuric acid per liter of pentane. The olefin-free pentane is then washed with an equal amount of water, dried over magnesium sulfate, distilled, and stored over sodium wire.

6. Ethyl trichloracetate (Eastman Kodak) is distilled prior to use.

7. The nitrogen flow must be slow enough to prevent significant loss of the pentane by evaporation.

8. A rotary evaporator is a convenient apparatus for this operation.

9. Distillation at significantly higher pressures results in increased decomposition.

3. Methods of Preparation

The present procedure is that described by the submitters.³

4. Merits of Preparation

The generation of dichlorocarbene for addition to olefins has been realized by the use of chloroform and alkali metal alkoxides^{4,5} (preferably potassium *tert*-butoxide), sodium trichloroacetate,⁶ butyllithium and bromotrichloromethane,⁷ and the reaction of an ester of trichloroacetic acid with an alkali metal alkoxide.^{2,3} The latter method, which is here illustrated by the preparation of 2-oxa-7,7-dichloronorcarane, generally gives higher yields of adducts.

¹ Department of Chemistry, University of Minnesota, Minneapolis 14, Minn.

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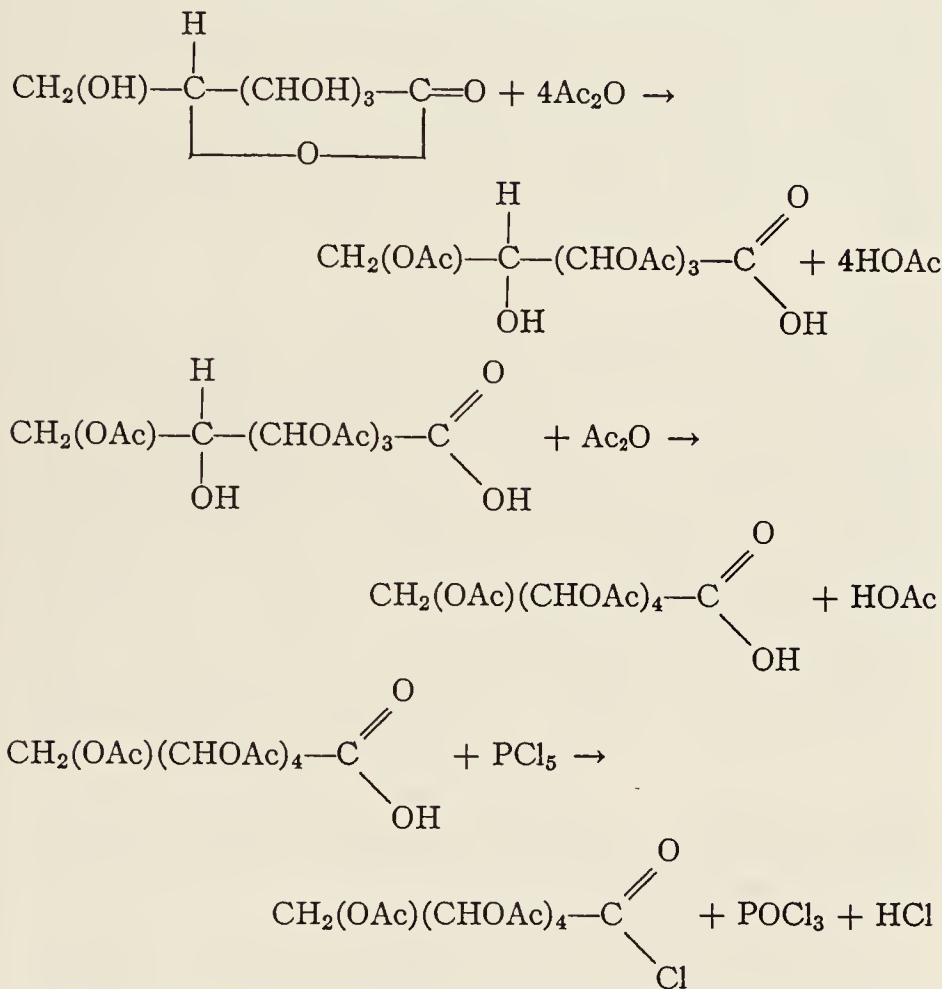
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**2,3,4,5,6-PENTA-O-ACETYL-D-GLUCONIC ACID AND
2,3,4,5,6-PENTA-O-ACETYL-D-GLUCONYL CHLORIDE**

(Gluconic acid, pentaacetyl-, D-, and
Gluconyl chloride, pentaacetyl-, D-)



Submitted by CHARLES E. BRAUN and CLINTON D. COOK.¹

Checked by W. G. WOODS, E. F. SILVERSMITH, and JOHN D. ROBERTS.

1. Procedure

A. *2,3,4,6-Tetra-O-acetyl-D-gluconic acid monohydrate*. Crushed, fused zinc chloride (20 g.) is shaken with 250 ml. of acetic anhydride in a 1-l. three-necked flask until most of the solid

dissolves. The flask is then equipped with mechanical stirrer, thermometer reaching into the liquid, and a dropping funnel. As the flask is cooled in an ice bath, 50 g. (0.28 mole) of D-glucono- δ -lactone (Note 1) is added slowly with vigorous stirring. During the addition, the temperature should be kept below 65°. After an hour in the ice bath, the solution is kept at room temperature for 24 hours and is then poured into 1 l. of water and stirred until the hydrolysis of the acetic anhydride is complete (about an hour). The mixture is placed in a refrigerator until the product crystallizes completely (Note 2). The crude material is removed by filtration and washed with a small amount of ice water. The 2,3,4,6-tetra-O-acetyl-D-gluconic acid monohydrate thus obtained melts at 113–117°. The yield is 79–84 g. (74–79%).

B. *2,3,4,5,6-Penta-O-acetyl-D-gluconic acid*. Tetra-O-acetyl-D-gluconic acid monohydrate (50 g., 0.13 mole) is slowly added to a chilled (0–5°) solution of 18 g. of fused zinc chloride in 190 ml. of acetic anhydride contained in a 1-l. Erlenmeyer flask. The solution is kept in an ice bath for an hour and then allowed to stand at room temperature for 24 hours. After dilution with 1 l. of water, the solution is extracted with four 100-ml. portions of chloroform. In order to remove the chloroform, 200 ml. is distilled, 250 ml. of toluene is added, and 250 ml. of this solution is distilled. Another 250 ml. of toluene is then added and the volume is reduced to 300 ml. The product crystallizes on standing at 0° (Note 2). The solid is removed by filtration, washed with toluene and then with petroleum ether (b.p. 35–55°). A yield of 44–45 g. (83–84%) of anhydrous 2,3,4,5,6-penta-O-acetyl-D-gluconic acid, melting at 110–111°, is obtained; $[\alpha]_D^{23} + 11.5^\circ$ ($c = 4.0$ in ethanol-free chloroform).

C. *2,3,4,5,6-Penta-O-acetyl-D-gluconyl chloride*. Anhydrous 2,3,4,5,6-penta-O-acetyl-D-gluconic acid (25 g., 0.062 mole) is shaken with 185 ml. of anhydrous ethyl ether in a 1-l. round-bottomed flask until most of the solid dissolves. Then 15 g. (0.072 mole) of phosphorus pentachloride is added with shaking. The flask is fitted with a calcium chloride drying tube and stored overnight at room temperature. Any solid material is removed by filtration through a fritted-glass funnel into a 1-l. round-

bottomed flask, and the ethereal solution is concentrated to about one-half volume under reduced pressure at room temperature. The concentrated solution is allowed to stand overnight at 0° or below. The mother liquor is decanted from the crystals, which are then broken up, transferred to a fritted-glass funnel, washed quickly with petroleum ether (b.p. 35–55°), and dried in a vacuum desiccator. The mother liquor is again concentrated to one-half its volume under reduced pressure and a second crop of crystals collected. The total yield of 2,3,4,5,6-penta-O-acetyl-D-gluconyl chloride, melting at 68–71° (Note 3), is 21–24 g. (80–92%), depending on the temperature of crystallization (Notes 4 and 5).

2. Notes

1. The D-glucono- δ -lactone (m.p. 153–155°; assay > 99%, Pfizer specification; water content < 0.2%, Karl Fischer titration) is obtained from Charles Pfizer & Co., Inc., 630 Flushing Avenue, Brooklyn 6, New York. Material having a water content greatly in excess of 0.2% may be dried for 48 hours at 100°. Drying at higher temperatures has in some samples produced decomposition. Independent experience with many preparations in the laboratories of one of the editors (Max Tishler, Merck Sharp & Dohme Research Laboratories) has indicated that drying is generally not necessary.

2. As long as 48 hours may be required.

3. The checkers found m.p. 69.5–74°.

4. Since 2,3,4,5,6-penta-O-acetyl-D-gluconyl chloride is appreciably soluble in ethyl ether at 0°, the yield can be improved by carrying out the crystallization at lower temperatures.

5. The submitters report $[\alpha]_D^{23} = +2.2$ ($c = 4.0$ in ethanol-free chloroform). The checkers found $[\alpha]_D^{25} = +2.5$.

3. Methods of Preparation

The method followed for the preparation of the two acids is a modification of that of Major and Cook.² The preparation for penta-O-acetyl-D-gluconyl chloride is that of Braun and co-workers.³ A slightly different technique has also been described.⁴

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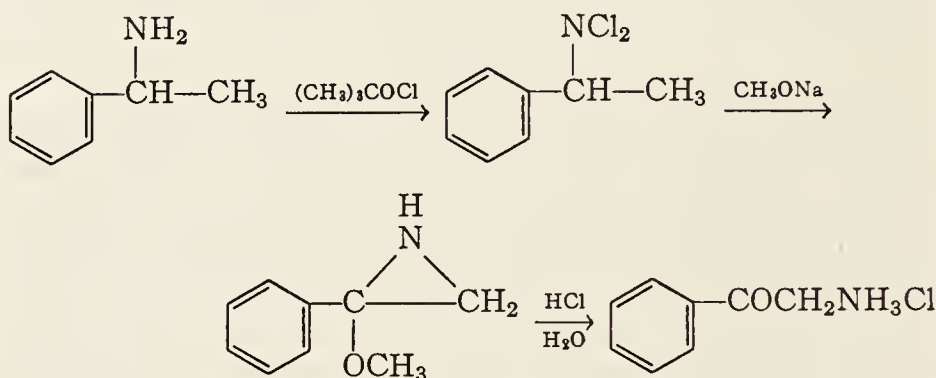
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PHENACYLAMINE HYDROCHLORIDE

(Acetophenone, 2-amino-, hydrochloride)



Submitted by HENRY E. BAUMGARTEN and
JAMES M. PETERSEN.¹

Checked by WILLIAM E. PARHAM, NORMAN NEWMAN and
R. M. DODSON.

1. Procedure

In a thoroughly dry 500-ml., three-necked, round-bottomed flask fitted with a mechanical stirrer, dropping funnel, and a Y-tube containing a calcium chloride drying tube and a thermometer (Note 1) are placed 24.2 g. (26 ml., 0.20 mole) of α -phenylethylamine (Note 2) and 50 ml. of dry benzene (Note 3). The solution is cooled in an ice-salt bath to 5°, and a solution of 44.5 g. (50 ml., 0.41 mole) of *tert*-butyl hypochlorite ² (Note 4) in 50 ml. of dry benzene (Note 3) is added at such a rate as to maintain the temperature below 10° (Note 5). After the addition of the *tert*-butyl hypochlorite solution is complete, the reaction mixture is stirred at room temperature 1–4 hours (Note 6).

The Y-tube is replaced by a reflux condenser fitted with a calcium chloride drying tube, and a freshly prepared solution of 13.8 g. (0.60 g. atom) of sodium in 140 ml. of anhydrous methanol (Note 7) is added to the benzene solution of N,N-dichloro- α -phenylethylamine at such a rate as to maintain gentle reflux (Note 8). After addition of the sodium methoxide is complete, the reaction mixture is heated under reflux until a test with acidified starch-iodide paper is negative (about 45–70 minutes) (Note 9). The reaction mixture is cooled in an ice-water bath, and the precipitated sodium chloride is removed by filtration through a Büchner funnel. The filter cake is washed with three 25-ml. portions of dry benzene. The combined filtrates are added very slowly with shaking or stirring to 150 ml. of 2*N* hydrochloric acid contained in a 1-l. beaker (Note 10). The layers are separated, and the benzene layer is extracted with three 50-ml. portions of 2*N* hydrochloric acid. The combined acid extracts are washed twice with 50-ml. portions of ether (Note 11). The ether extracts are discarded. The pale amber to yellow aqueous solution is evaporated to dryness at a temperature not greater than 40° (Note 12). The residue is transferred to a 1-l. round-bottomed flask fitted with a reflux condenser to which is added 400 ml. of isopropyl alcohol-hydrochloric acid solution (Note 13). The mixture is heated under reflux for at least 30 minutes and is filtered hot through a Büchner funnel. The residual solid is returned to the flask and extracted in the same manner with a 150-ml. portion of the isopropyl alcohol-hydrochloric acid solution. The solid residue (sodium chloride) is discarded (Note 14). The two extracts are cooled separately in the refrigerator overnight and then filtered on a Büchner funnel (Note 15). The nearly colorless crystals are washed on the filter with two 50-ml. portions of dry ether. Each of the filtrates is diluted with an equal volume of dry ether (400 ml. and 150 ml., respectively) and is allowed to stand in the refrigerator overnight. From these diluted filtrates additional crops of crystals are collected (Note 16). The combined yield of the three to four crops is 18.9–24.8 g. (55–72%), m.p. 185–186° dec. (Notes 17 and 18). Normally the product is sufficiently pure for use without further purification; however, the product may be recrystallized from isopropyl

alcohol-hydrochloric acid solution (Note 12), using 100 ml. of the solution for each 6 g. of compound. The recovery is about 5.5 g. per 6.0 g. of crude product.

2. Notes

1. The submitters used apparatus with ground-glass joints and dried the various pieces in the oven at 120–140° overnight before use. The Y-tube was constructed from a 24/40 male joint by joining a short length of 8-mm. i.d. glass tubing to the unground end of the joint in such a fashion as to permit insertion of a thermometer through the joint into the flask and then joining a second short piece of 8-mm. i.d. glass tubing in such a fashion as to permit attachment of a calcium chloride tube without interfering with the thermometer opening. If desired, a four-necked flask may be substituted for the Y-tube and three-necked flask.

2. The submitters used *dl*- α -phenylethylamine obtained either from the Eastman Kodak Company or Matheson, Coleman and Bell without further purification. The preparation of *dl*- α -phenylethylamine has been described previously in *Organic Syntheses*.^{3,4}

3. Reagent grade dry benzene is dried by simple distillation, the first 10% of the distillate being discarded.

4. The submitters did not redistil the *tert*-butyl hypochlorite. If it is desired to avoid the use of *tert*-butyl hypochlorite, an equivalent quantity of dichloramine B (N,N-dichlorobenzene-sulfonamide, Arapahoe Chemical Co., Boulder, Colorado) may be substituted. This material is soluble in benzene but the benzene-sulfonamide is not; therefore the reaction mixture must be filtered just before the addition of the sodium methoxide solution. Using this technique, the submitters obtained 44–52% of phenacylamine hydrochloride.

5. The rate of addition is not critical, for the reaction is not especially exothermic. However, at even slightly elevated temperatures the N,N-dichloroamines may begin to decompose with the formation of undesired products; therefore the addition can be carried out as rapidly as desired within the specified temperature range. With a reasonable cooling efficiency this will be

well below 30 minutes, but no harm will be done if a longer period is required.

6. The halogenation reaction appears to be quite rapid; therefore the time of stirring is not critical but probably should not be prolonged beyond 4 hours. The submitters used this time interval to prepare the sodium methoxide solution, and the actual time lapse depended upon the time required to prepare this solution. The solution of N,N-dichloro- α -phenylethylamine should be clear yellow after the stirring period. A turbid solution or one containing a precipitate usually indicates a poor sample of *tert*-butyl hypochlorite.

7. Commercial absolute methanol is dried by heating the material under reflux over magnesium turnings for 4 hours, followed by distillation into a dried receiver. Normally 1 g. of magnesium turnings per 100 ml. of absolute methanol will be sufficient. To allow for losses during the drying and distillation, the charge of methanol should be at least twice the amount required for the preparation.

It is advantageous to dry the methanol the day before the preparation is to be carried out and to store the dried methanol in a carefully sealed, *dry* flask or to allow the methanol-magnesium mixture to reflux overnight followed by distillation just prior to use.

The submitters used the inverse addition procedure for preparing the methanolic sodium methoxide, as follows. In a thoroughly dry 500-ml., three-necked, round-bottomed flask fitted with a mechanical stirrer, dropping funnel, and a reflux condenser carrying a calcium chloride drying tube is placed 13.8 g. (0.60 g. atom) of sodium freshly cut into small pieces. To this is added slowly 140 ml. of anhydrous methanol at such a rate as to maintain vigorous reflux. If all the sodium does not dissolve during the addition of the methanol, the mixture may be heated on the steam bath until solution is effected or additional methanol (up to 25 ml.) may be added. The preparation of the solution of sodium methoxide requires about 30 minutes.

It may be advantageous to allow a slow stream of dry nitrogen to pass through the apparatus during the addition of the methanol. The submitters routinely omit this precaution and, as yet,

have experienced no accidents or fires. For other precautions see Note 1, *Org. Syntheses*, Coll. Vol. 3, 215 (1955).

8. The rate of addition probably is not critical but should not be allowed to proceed uncontrolled. The submitters added the sodium methoxide solution at such a rate as to cause vapors of the refluxing methanol to condense in the first 2–3 in. of the reflux condenser without application of external heating.

9. A positive test is the immediate formation of a dark violet or brown spot on starch-iodide paper moistened with 2*N* hydrochloric acid. A negative test may consist of a very faint beige color or complete absence of color.

10. The reverse mode of addition may lower the yield and introduce unwanted condensation products of the amino ketone, which is not stable in neutral or alkaline solution.

11. The procedure should be continued up to at least this point without stopping. After this operation the sequence may be interrupted at any time.

If the *tert*-butyl hypochlorite has been prepared in advance and if the methanol to be used has been allowed to reflux over magnesium overnight, the solvents can be distilled and the reaction carried to this point in an 8-hour day. However, it may be preferable to prepare the dry solvents the day before the reaction is to be run. The latter procedure appears to have little effect on the final yield provided that the solvents are stored in tightly sealed containers and transferred with due care.

12. The submitters strongly recommend the use of a rotating evaporator (such as the Flash-Evaporator, Laboratory Glass Supply Co., New York 31, N. Y.) with which the solution can be reduced to a syrup in about 4 hours. The further evaporation is facilitated by adding 100 ml. of commercial absolute ethanol at this point and continuing the evaporation. Total time for evaporation will be about 6 hours, and the product will be a crystalline mass. The extraction step may be carried out in the 2-l. flask normally used with the evaporator.

If a rotating evaporator is not available, the solution is poured into a large porcelain evaporating dish and is allowed to stand protected in the hood for several days. Toward the end of this time, the evaporation may be accelerated by the addition of 100

ml. of ethanol as described above. The checkers removed water by blowing air over the solution.

13. The isopropyl alcohol-hydrochloric acid solution contains 1 ml. of concentrated hydrochloric acid per 100 ml. of isopropyl alcohol. If the hydrochloric acid is omitted, the product will be impure and the yield greatly reduced. Sodium chloride is not appreciably soluble in this solution.

14. The yield of sodium chloride is usually 33–35 g. (94–100%). It is often helpful to recover and weigh the sodium chloride before discarding it. An excess over the theoretical amount indicates incomplete extraction.

15. If the reflux period has been sufficiently long, little or no precipitate will be formed at this stage in the second extracting solution, which is used to ensure efficient extraction.

16. At this stage, crops of crystals may be formed in each solution.

TABLE I

PREPARATION OF α -AMINO KETONES

Product	Approx. Reaction Time, ^a min.	Yields, %	Recryst. Solvent	M.P., °C. ^b
Hydrochloride of				
2-Aminocyclopentanone	180	34–36	<i>i</i> -PrOH	146–147
2-Aminocyclohexanone	25–45	49–73	<i>i</i> -PrOH	156
3-Amino-2-heptanone	210	50–75	<i>i</i> -PrOH	134–135
<i>p</i> -Bromophenacylamine	70	58–73	2 <i>N</i> HCl	275
<i>p</i> -Chlorophenacylamine	80–90	49–60	EtOH	270–271
<i>p</i> -Methoxyphenacylamine	270	62–74	EtOH	200
<i>p</i> -Nitrophenacylamine	60	50–56	MeOH	243
<i>p</i> -Methylphenacylamine	80–90	70–72	<i>i</i> -PrOH	206–207
<i>p</i> -Phenylphenacylamine	80	54–71	2 <i>N</i> HCl	185–186
α -Aminovalerophenone	30	65–66	<i>i</i> -PrOH-Et ₂ O	156.5–158
2-Amino-1-tetralone	100	63–70	<i>i</i> -PrOH	201–202
2-Amino-4,4-dimethyl-1-tetralone	300	61–65	<i>i</i> -PrOH	212–213
Desylamine (2-amino-2-phenylacetophenone)	30	45–46	<i>i</i> -PrOH	233–234
Phenacylamine	45–70	55–78	<i>i</i> -PrOH	185–186

^a Time for negative starch-iodide test.

^b Usually with decomposition.

17. Further treatment of the filtrate normally will yield little crystalline material.

18. The submitters report that, on the basis of experience in student preparations courses, the usual percentage yields for fairly capable technicians on their first trial are in the low fifties, and on subsequent trials in the sixties. Persons with exceptionally good laboratory technique may get even greater yields than those specified (up to 78%).

This procedure may be used for the preparation of a variety of α -amino ketones as is indicated in Table I, which summarizes most of the submitters' experience with this reaction. Principal deviations from the procedure will be in the time required for a negative starch-iodide test and the nature and amount of extraction and recrystallization solvent. *It is strongly recommended that any one using the reaction for the first time carry out the preparation on α -phenylethylamine before attempting to use it on other more valuable amines.*

3. Methods of Preparation

Phenacylamine hydrochloride has been prepared by (1) the hydrolysis of the quaternary salt obtained from phenacyl bromide and hexamethylenetetramine (the Delepine reaction),⁵⁻¹¹ (2) the hydrolysis of N-phenacylphthalimide (the Gabriel reaction),¹²⁻¹⁴ (3) the reduction or catalytic hydrogenation of α -oximinoacetophenone,^{10, 15-19} (4) the reduction of α -nitroacetophenone,^{20, 21} (5) the catalytic hydrogenation of α -azidoacetophenone,²² (6) the catalytic hydrogenation of α -benzylaminoacetophenone,²³ (7) the base-catalyzed rearrangement of the tosylate of acetophenone oxime (the Neber rearrangement),^{24, 25} (8) the base-catalyzed rearrangement of acetophenone dimethylhydrazone methiodide,²⁶ (9) the Friedel-Crafts acylation of benzene with glycyl chloride hydrochloride,²⁷ as well as by other procedures of uncertain preparative value. The present procedure is adapted from those of Baumgarten and Bower¹⁹ and Baumgarten and Petersen.²⁸

4. Merits of the Preparation

The present procedure is a specific example of a synthetic method of some generality. The procedure describes an example which is of considerable interest *per se* but, perhaps more importantly, which also serves as a model for the use of this procedure for the preparation of other α -amino ketones. In the submitters' laboratory, this specific procedure is used routinely for the training of persons who will be using this general technique or related techniques.²⁹

Of the procedures cited in Section 3, procedures (1), (3), and (4) have been examined by the submitters for comparison with the present procedure. Of these, the present procedure and that based on the Delepine reaction (1) appeared to be the most satisfactory for preparative purposes. Yields by the two procedures were comparable; however, the Delepine reaction could be run somewhat more conveniently on a larger scale (provided that one was willing to accept a tedious extraction of the product from the copious quantity of ammonium salts with which it is mixed). The Delepine reaction also makes a lesser demand on the skill and technique of the operator. On the other hand, attempts in the submitters' laboratory to extend the Delepine reaction to *sec*-bromides have been unsuccessful; therefore the Delepine reaction appears to lack the generality of the present procedure, which shares such generality, apparently, with procedures (2), (3), (7), and (8). Furthermore, the Delepine reaction gives a mixture of phenacylamine hydrochloride and hydrobromide^{5,10} (although the submitters have found that by careful fractional crystallization from isopropyl alcohol-hydrochloric acid solution about 50% of the pure hydrochloride can be obtained).

¹ Avery Laboratory, University of Nebraska, Lincoln 8, Neb. This work was supported in part by grants G-1090 and G-11339 of the National Science Foundation.

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Phenyl *tert*-Butyl Ether

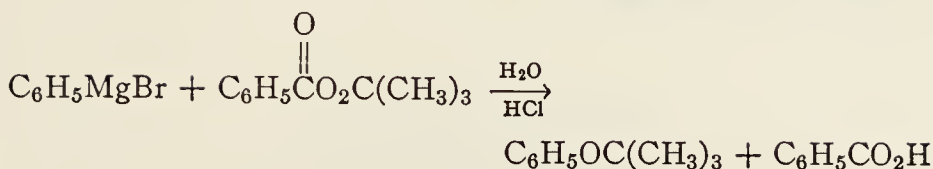
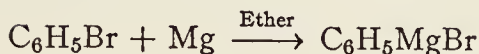
CORRECTIONS

Line 14 of the Procedure (page 91) should read:

anhydrous ether is added. A solution of 58.3 g. (0.3 mole, 56

Note 1 (page 92) should read:

1. *tert*-Butyl perbenzoate is supplied by Lucidol Division, Wallace and Tiernan Inc., Buffalo 5, New York, or L. Light & Co., Ltd., Colnbrook, Bucks, England. The Lucidol product contains 98% *tert*-butyl perbenzoate.

PHENYL *tert*-BUTYL ETHER(Ether, *tert*-butyl phenyl)Submitted by CHRISTER FRISSELL and SVEN-OLOF LAWESSON.¹

Checked by WILLIAM G. DAUBEN and GILBERT H. BEREZIN.

1. Procedure

A 1-l., three-necked, round-bottomed flask equipped with a sealed mechanical stirrer, a reflux condenser, and a 500-ml. pressure-equalized dropping funnel is arranged for conducting a reaction in an atmosphere of nitrogen by fitting into the top of the condenser a T-tube attached to a low-pressure supply of nitrogen and to a mercury bubbler. The flask is dried by warming with a soft flame as a slow stream of nitrogen is passed through the system. In the cooled flask a solution of phenylmagnesium bromide is prepared from 13 g. (0.53 g. atom) of magnesium turnings, 79 g. (0.5 mole, 53.6 ml.) of bromobenzene, and 200 ml. of anhydrous ether.

After the preparation of phenylmagnesium bromide is complete, the ethereal solution is cooled in an ice bath and 200 ml. of anhydrous ether is added. A solution of 58.3 g. (0.3 mole, 39.0 ml.) of *tert*-butyl perbenzoate (Note 1) in 120 ml. of anhydrous ether is added, dropwise, with stirring over a 30-minute period, and the stirring is continued for an additional 5 minutes.

The reaction mixture is poured carefully into a cold solution of 40 ml. of concentrated hydrochloric acid in 1 l. of water. The ethereal layer is separated, and the aqueous layer is extracted

twice with 150-ml. portions of ether. The combined organic layers are extracted with three 25-ml. portions of 2*M* sodium hydroxide solution, washed with water until the washings are neutral, and then dried over anhydrous magnesium sulfate (Notes 2 and 3). The dried solution is concentrated and the product distilled under reduced pressure, b.p. 57–59°/7 mm. The yield of phenyl *tert*-butyl ether is 35–38 g. (78–84%), n_D^{20} 1.4870–1.4880. This synthetic process is applicable to the preparation of other *tert*-butyl ethers (Note 4).

2. Notes

1. *tert*-Butyl perbenzoate is supplied by Lucidol Division, Wallace and Tiernan Inc., Buffalo 5, New York.

2. The ethereal solution should be tested for peroxides as follows: A few milligrams of sodium iodide, a trace of ferric chloride, and 3 ml. of glacial acetic acid are placed in a test tube and 2 ml. of the ether solution added carefully. When unconsumed perbenzoate is present, a yellow ring is formed immediately between the two phases. If a positive test is obtained, the acid and base treatments should be repeated.

3. By acidification of the sodium hydroxide solution, 29–32 g. of benzoic acid (80–90%) is obtained.

4. The same general method has been used by the submitters to prepare *o*-tolyl *tert*-butyl ether, *m*-tolyl *tert*-butyl ether, benzyl *tert*-butyl ether, and *p*-anisyl *tert*-butyl ether.

3. Methods of Preparation

The method presented is essentially that described by Lawesson and Yang.² Phenyl *tert*-butyl ether has been prepared by acid-catalyzed condensation of isobutylene and phenol³ and by reaction of diphenyliodonium chloride with potassium *tert*-butoxide.⁴

4. Merits of Preparation

The synthesis of *tert*-butyl ethers by the reaction of Grignard reagents with *tert*-butyl perbenzoate appears to have considerable

generality (Note 4), and the perester is a stable, readily available material.

¹ Department of Chemistry, University of Uppsala, Uppsala, Sweden.

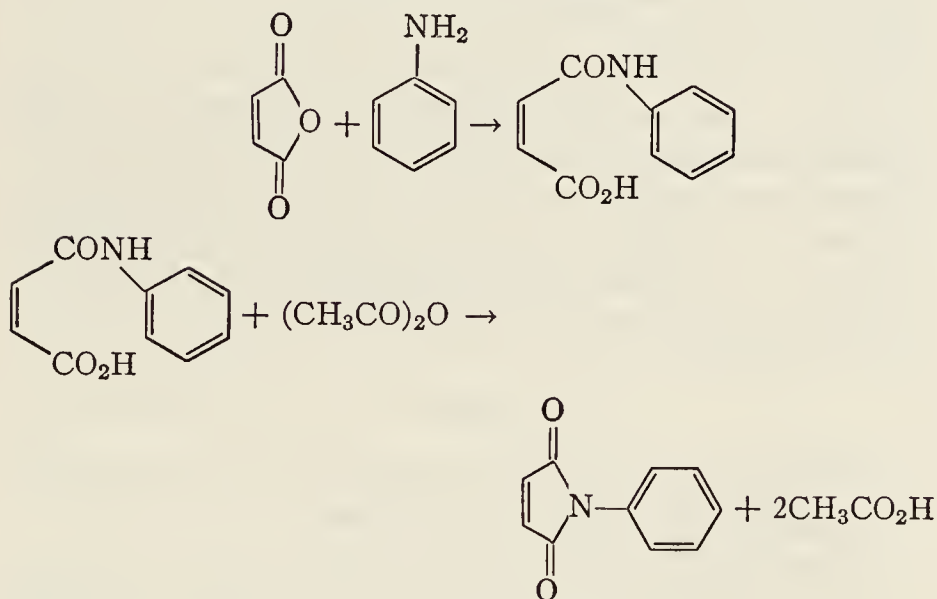
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N-PHENYLMALEIMIDE

(Maleimide, N-phenyl-)



Submitted by M. P. CAVA, A. A. DEANA, K. MUTH, and
M. J. MITCHELL.¹

Checked by CAROLE L. OLSON, MARJORIE C. CASERIO,
and JOHN D. ROBERTS.

1. Procedure

A. *Maleanilic acid*. In a 5-l. three-necked flask provided with a paddle-type stirrer, a reflux condenser, and a dropping funnel are placed 196 g. (2 moles) of maleic anhydride (Note 1) and

2.5 l. of ethyl ether (Note 2). The stirrer is started and, when all the maleic anhydride has dissolved, a solution of 182 ml. (186 g., 2 moles) of aniline (Note 3) in 200 ml. of ether (Note 2) is run in through the dropping funnel (Note 4). The resulting thick suspension is stirred at room temperature for 1 hour and is then cooled to 15–20° in an ice bath. The product is obtained by suction filtration. It is a fine, cream-colored powder, m.p. 201–202°, suitable for use in the next step without purification. The yield is 371–374 g. (97–98%).

B. *N*-Phenylmaleimide. In a 2-l. Erlenmeyer flask are placed 670 ml. of acetic anhydride (Note 5) and 65 g. of anhydrous sodium acetate. The maleanilic acid (316 g.), obtained as described above, is added, and the resulting suspension is dissolved by swirling and heating on a steam bath for 30 minutes (Note 6). The reaction mixture is cooled almost to room temperature in a cold water bath and is then poured into 1.3 l. of ice water. The precipitated product is removed by suction filtration, washed three times with 500-ml. portions of ice-cold water and once with 500 ml. of petroleum ether (b.p. 30–60°), and dried. The yield of crude *N*-phenylmaleimide is 214–238 g. (75–80%), m.p. 88–89°. Recrystallization from cyclohexane gives canary-yellow needles, m.p. 89–89.8° (Note 7).

2. Notes

1. Reagent grade maleic anhydride is used without purification.
2. Reagent grade anhydrous ether is used.
3. Reagent grade aniline is used without further purification.
4. The aniline solution may be run in as fast as is possible without flooding the condenser.
5. Carbide and Carbon or Baker's Analyzed technical grade acetic anhydride is used.
6. The sodium acetate fails to dissolve completely.
7. About 500 ml. of the refluxing solvent will dissolve some 58 g. of *N*-phenylmaleimide. The recovery of recrystallized material is approximately 93%.

3. Methods of Preparation

The procedure described here is based on a method outlined in U. S. patent 2,444,536.² N-Phenylmaleimide has also been prepared by the dry distillation of the aniline salt of malic acid,^{3,4} by treating the aniline salt of malic acid with phosphorus pentoxide,⁵ and by treating maleanilic acid with phosphorus trichloride or with phosphorus pentoxide.⁶ Ring-substituted N-phenylmaleimides, viz., N-(*p*-methoxyphenyl)-, N-(*p*-ethoxyphenyl)-, and N-(*p*-nitrophenyl)maleimide, have been prepared by treatment of the appropriate maleanilic acids with acetic anhydride and fused potassium acetate.⁷

4. Merits of Preparation

N-Phenylmaleimide is an active dienophile in the Diels-Alder reaction and usually gives crystalline adducts.

¹ Chemistry Department, The Ohio State University, Columbus 10, Ohio.

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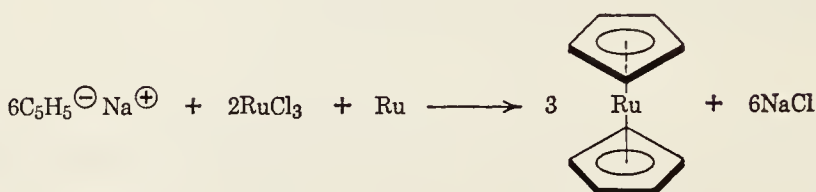
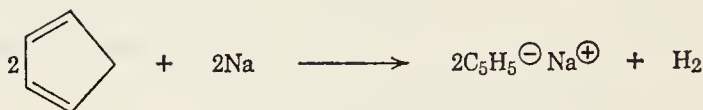
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RUTHENOCENE

(Ruthenium, dicyclopentadienyl-)



Submitted by D. E. BUBLITZ, WILLIAM E. MCEWEN, and
JACOB KLEINBERG.¹

Checked by HANS G. ESSLER and JOHN H. RICHARDS.

1. Procedure

A 500-ml. three-necked flask is equipped with a Trubore stirrer, reflux condenser, and a pressure-equalizing dropping funnel that carries an inlet for admission of nitrogen. The system is purged with nitrogen (Note 1), and 300 ml. of 1,2-dimethoxyethane (Note 2) is added, followed by 7.2 g. (0.312 g. atom) of sodium either as wire or freshly cut small pieces. The solution is stirred, and 31.0 ml. (0.376 mole) of cyclopentadiene (Note 3) is added dropwise. When the evolution of hydrogen has almost ceased, the mixture is maintained at slightly below the reflux temperature for 1–2 hours. In the event that all the sodium does not dissolve, the solution is cooled to room temperature, a few milliliters more of cyclopentadiene added, and the mixture heated again until dissolution of the sodium is complete.

A mixture of 14.6 g. (0.07 mole) of ruthenium trichloride and 2.4 g. (0.024 g. atom) of ruthenium metal (Note 4) is added, and the reaction mixture is heated and stirred under nitrogen for 80

hours (Note 5) at slightly below the reflux temperature. With the use of stirring, the solvent is removed at aspirator pressure, and the flask then refilled with nitrogen. The solid is transferred to a sublimator in a dry-box containing a nitrogen atmosphere (Note 6) and sublimed at 0.1 mm. pressure with a heating bath at 130° (Note 7). The sublimate is dissolved in benzene and passed through a 1 x 12-in. column of activated alumina. Evaporation of the benzene gives 12.2–15.1 g. (56–69%) of ruthenocene, m.p. 199–200° (Note 8).

2. Notes

1. The submitters used prepurified nitrogen, obtained from Matheson Company, Inc., East Rutherford, New Jersey, without further purification. The checkers passed Linde (H. P. Dry) nitrogen successively through chromous chloride solution, solid potassium hydroxide, Ascarite, and solid phosphorus pentoxide.

2. 1,2-Dimethoxyethane is dried over sodium wire and then distilled under nitrogen from lithium aluminum hydride just before use.

3. For preparation of cyclopentadiene from the dimer, see G. Wilkinson, *Org. Syntheses*, **36**, 31 (1956). The dicyclopentadiene used as starting material was dried by passage through a 1 x 12-in. column of activated alumina prior to cracking.

4. Ruthenium trichloride was prepared by chlorination of powdered ruthenium at 650–700°² with the use of metal obtained from Goldsmith Bros. Smelting and Refining Co., 111. N. Wabash Ave., Chicago 2, Illinois. Complete chlorination could not be effected under these conditions, and on the average about 85% of the metal was converted to trichloride. Consequently, in all the preparations of ruthenocene, mixtures of trichloride and metal, as obtained from the chlorination reaction, were employed. The equations given for the preparation are idealized; the submitters believe that during the course of reaction the trichloride is gradually reduced to dichloride by ruthenium metal, and that it is the dichloride which reacts with sodium cyclopentadienide.

5. Somewhat lower yields than those reported are obtained when the reaction is carried out for a shorter period of time.

6. From this point on, the solid materials are pyrophoric, especially the residual solids from the sublimation process. However, the ruthenocene obtained by sublimation is not pyrophoric. The checkers found that careful addition of the sublimation residues to water under nitrogen destroys their pyrophoric character.

7. The checkers found the use of a Dry Ice-cooled sublimation finger advantageous.

8. The yield reported here is based on the total amount of ruthenium (both Ru^{III} and Ru^0) available for formation of ruthenocene. An additional quantity of ruthenocene may be obtained by extraction of the pyrophoric residue from the sublimation step with benzene in a Soxhlet extractor under a nitrogen atmosphere. The benzene solution is filtered through activated alumina, the solvent evaporated, and the residue sublimed.

3. Methods of Preparation

Ruthenocene has been prepared in 20% yields by reaction of cyclopentadienylmagnesium bromide with ruthenium(III) acetylacetonate.³ More recently,⁴ the compound has been made in 43–52% yield by treatment of sodium cyclopentadienide with ruthenium trichloride in tetrahydrofuran or 1,2-dimethoxyethane.

4. Merits of the Preparation

Ruthenocene is an example of a stable π -bonded organometallic compound which undergoes substitution reactions similar to those displayed by ferrocene. Because ruthenocene has heretofore been relatively unavailable, its chemistry has not been extensively studied.

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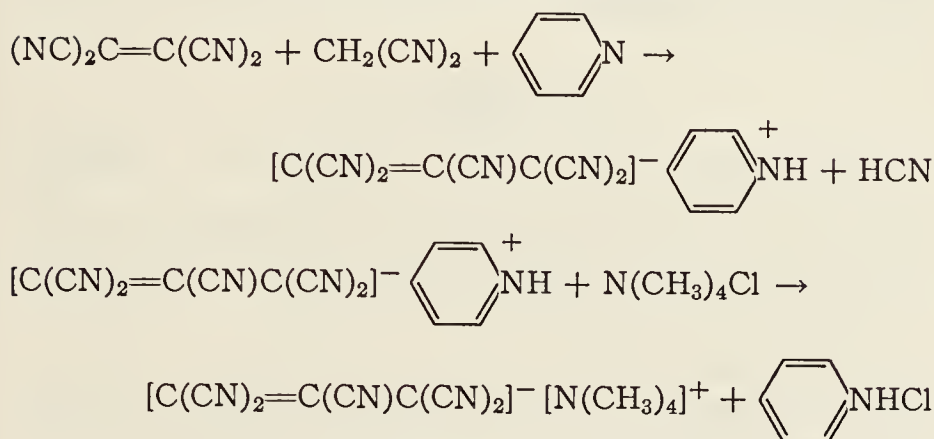
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**TETRAMETHYLAMMONIUM
1,1,2,3,3-PENTACYANOPROPENIDE**

(1-Propene-1,1,2,3,3-pentacarbonitrile,
tetramethylammonium salt)



Submitted by W. J. MIDDLETON and D. W. WILEY.¹

Checked by JAMES CASON and WILLIAM T. MILLER.

1. Procedure

Caution! This reaction must be carried out in an efficient hood because large amounts of hydrogen cyanide are evolved. It is also recommended that tetracyanoethylene not be allowed to come into contact with the skin.

A solution of 6.6 g. (0.10 mole) of malononitrile (Note 1) in 8.7 g. (0.11 mole) of pyridine and 25 ml. of water is prepared in a 125-ml. Erlenmeyer flask and stirred mechanically (no stirrer seal required) as there is added rapidly in small portions a total of 12.8 g. (0.10 mole) of powdered recrystallized tetracyanoethylene.² The resulting mixture is warmed on a hot plate as stirring is continued until complete solution occurs (5–10 minutes, Note 2). The hot dark solution is poured into a swirled solution of 12.1 g. (0.11 mole) of tetramethylammonium chloride (Note 3) in 500 ml. of water. The resultant mixture is heated almost to

boiling to give a dark-red solution, which is then allowed to cool spontaneously to room temperature. After final cooling in an ice bath, the orange needles of tetramethylammonium 1,1,2,3,3-pentacyanopropenide are collected by suction filtration and washed with two 100-ml. portions of cold water. This product is dissolved in 500 ml. of hot water, decolorized with about 5 g. of activated carbon, and allowed to crystallize as described above. The yield of bright yellow-orange needles, m.p. 314–315° (Note 4), is 19.5–20.5 g. (81–85%).

2. Notes

1. Malononitrile, m.p. 30–31°, obtained from Winthrop-Stearns Corp., New York, N. Y., is satisfactory.

2. The rate of solution depends upon the fineness of the tetracyanoethylene powder; however, solution should occur soon after the temperature reaches 60–70°.

3. A technical grade of tetramethylammonium chloride is satisfactory, provided old samples that have absorbed considerable water are not used.

4. In a heated block, the checkers observed melting points in the range 318–321°.

3. Methods of Preparation

Tetramethylammonium 1,1,2,3,3-pentacyanopropenide has been prepared by the base-catalyzed hydrolysis of tetracyanoethylene,³ and by the present method, which is more economical of tetracyanoethylene.

4. Merits of Preparation

Tetramethylammonium 1,1,2,3,3-pentacyanopropenide is useful for preparation of pentacyanopropenide salts of other metal and quaternary ammonium cations by metathesis.³ The free acid, which may be obtained by use of an ion-exchange resin,³ has an ionization constant comparable to that of a strong mineral acid ($\text{pK}_a < -8.5$; the anion is not detectably protonated in 12*M* sulfuric acid).⁴

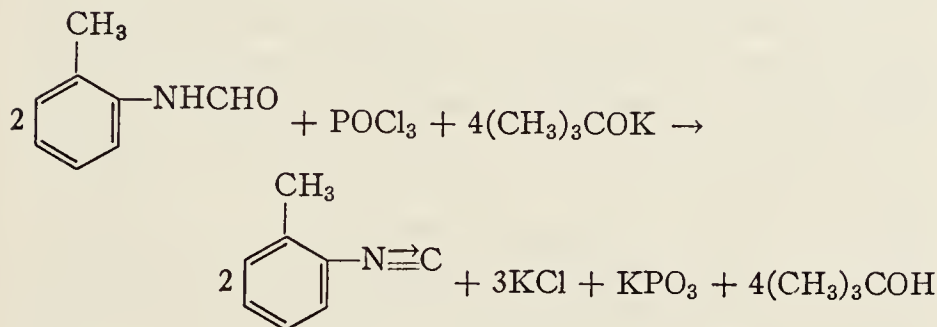
¹ Contribution No. 482 from Central Research Department, Experimental Station, E. I. du Pont de Nemours and Co., Wilmington, Delaware.

² R. A. Carboni, *Org. Syntheses*, **39**, 64 (1959).

³ W. J. Middleton, E. L. Little, D. D. Coffman, and V. A. Engelhardt, *J. Am. Chem. Soc.*, **80**, 2795 (1958).

⁴ R. H. Boyd, unpublished experiments.

o-TOLYL ISOCYANIDE



Submitted by IVAR UGI and RUDOLF MEYER.¹

Checked by B. C. McKUSICK and O. W. WEBSTER.

1. Procedure

Caution! Isocyanides should be prepared in a hood since they have unpleasant odors and are toxic.

The reaction is conducted in a 2-l. round-bottomed flask equipped with a dropping funnel, Hershberg stirrer, thermometer, and reflux condenser. A T-tube attached to a cylinder of dry nitrogen is inserted in the top of the condenser in order to keep the reaction mixture blanketed with nitrogen.

A suspension of potassium *tert*-butoxide is prepared by a slight modification of the procedure of Johnson and Schneider,² *particular attention being paid to the precautions they recommend for safe handling of potassium*. Dry *tert*-butyl alcohol (1250 ml.) is distilled directly into the reaction flask under nitrogen. One hundred grams (2.6 g. atoms) of potassium cut into about ten pieces is added. The stirred mixture spontaneously warms to the melting

point of potassium (62°) in the course of 15–60 minutes, whereupon the metal disperses into droplets. As the potassium gradually dissolves, the temperature of the mixture rises to the boiling point of *tert*-butyl alcohol. The rate of solution of the potassium should be such that the *tert*-butyl alcohol refluxes gently, and this rate is regulated by the speed of stirring. If the boiling becomes too vigorous, the stirring is stopped completely, and if necessary the reaction vessel is cooled by immersion in a bath of cold oil kept in readiness for this purpose. Potassium *tert*-butoxide gradually precipitates, and the mixture is a thick suspension when all the potassium has reacted (Note 1).

N-*o*-Tolylformamide (135 g., 1.00 mole) (Note 2) is added to the hot stirred suspension, which becomes a clear solution within a few minutes. The solution is cooled to 10 – 20° by means of an ice bath and maintained at this temperature while 92 g. (0.60 mole) of phosphorus oxychloride is added to it with stirring over the course of 30–40 minutes. The reaction mixture is stirred at 30 – 35° for 1 hour and poured into an ice-cold stirred solution of 50 g. of sodium bicarbonate in 5 l. of water (Note 3). *o*-Tolyl isocyanide precipitates as an oil. It is taken up in 300 ml. of petroleum ether (b.p. 40 – 60°), and the organic phase is separated in a separatory funnel. The aqueous phase is extracted with three 200-ml. portions of petroleum ether. The combined extracts are washed with 50 ml. of 5% sodium bicarbonate solution, dried over 50 g. of powdered potassium hydroxide, and distilled through a 30-cm. vacuum-jacketed Vigreux column. *o*-Tolyl isocyanide is collected as a colorless, vile-smelling liquid at 61 – $63^{\circ}/10$ mm.; n_D^{25} 1.5212–1.5222; weight 74–85 g. (63–73%) (Note 4).

2. Notes

1. In order to keep down the volume of the reaction mixture, less *tert*-butyl alcohol is used than is necessary to dissolve the potassium *tert*-butoxide.

2. The checkers prepared *N*-*o*-tolylformamide³ as follows. A solution of 100 g. (0.94 mole) of *o*-toluidine and 82 ml. (100 g., 2.13 moles) of 98% formic acid in 300 ml. of toluene is refluxed under a condenser attached to a water separator.⁴ After water

stops collecting in the separator (about 3 hours), toluene and excess formic acid are removed by distillation under reduced pressure. The crude N-*o*-tolylformamide that remains is recrystallized from toluene to give 95–101 g. (75–80%) of N-*o*-tolylformamide, m.p. 60/61°. If a formamide that melts above the boiling point of *tert*-butyl alcohol is to be converted to an isocyanide by the present procedure, it should be finely pulverized.

3. *o*-Tolyl isocyanide is rather unstable, and in order to get a good yield one should work up the reaction mixture as quickly as possible and avoid unnecessary heating of the crude isocyanide. If the isocyanide is to be stored for a long time, it should be kept at the temperature of Dry Ice.

4. The equipment used in this preparation can be freed of the disagreeable odor of *o*-tolyl isocyanide by being washed with 5% methanolic sulfuric acid.

3. Methods of Preparation

o-Tolyl isocyanide has been prepared in 20% yield by the action of chloroform and potassium hydroxide on *o*-toluidine.⁵ The present procedure⁶ gives much better results.

4. Merits of Preparation

This procedure illustrates the best way to prepare aryl isocyanides. It is quite general, having been used by Ugi and Meyr⁶ to make the following isocyanides from the corresponding formamides: phenyl (56%), *p*-tolyl (66%), 2,6-dimethylphenyl (88%), mesityl (80%), *o*-chlorophenyl (43%), *p*-chlorophenyl (54%), 2-chloro-6-methylphenyl (87%), *p*-methoxyphenyl (64%), *p*-diethylaminophenyl (75%), *p*-nitrophenyl (41%), and 2-naphthyl (50%). Aliphatic isonitriles are generally best prepared by a simpler procedure involving the action of phosphorus oxychloride on an N-alkylformamide in the presence of pyridine.⁷

¹ Institute of Organic Chemistry, University of Munich, Munich, Germany.

² W. S. Johnson and W. P. Schneider, *Org. Syntheses*, **30**, 18 (1950).

³ A. Ladenburg, *Ber.*, **10**, 1123 (1877).

⁴ S. Natelson and S. Gottfried, *Org. Syntheses*, Coll. Vol. **3**, 381 (1955).

⁵ J. U. Nef, *Ann.*, **270**, 309 (1892).

⁶ I. Ugi and R. Meyr, *Chem. Ber.*, **93**, 247 (1960).

⁷ I. Ugi, R. Meyr, M. Lipinski, F. Bodesheim, and F. Rosendahl, this volume, p. 13.

1,1,1-TRIFLUOROHEPTANE

(Heptane, 1,1,1-trifluoro-)



Submitted by W. R. HASEK.¹

Checked by JOHN E. BALDWIN and JOHN D. ROBERTS.

1. Procedure

Caution! Sulfur tetrafluoride is toxic. This procedure should be carried out in a good hood. The pressure vessel should be heated in a well-ventilated area.

Twenty-six grams (0.20 mole) of heptanoic acid is placed in a 145-ml. pressure vessel lined with Hastelloy-C (Note 1). The air in the vessel is displaced with nitrogen, and the head of the vessel is secured in place. The vessel is cooled in a bath of acetone and solid carbon dioxide, and the nitrogen in the vessel is evacuated with a vacuum pump to a pressure of 0.5–1.0 mm. Sixty-five grams (95% pure, 0.57 mole) of sulfur tetrafluoride (Note 2) is transferred to the cold vessel. This is conveniently done by connecting a cylinder containing 65 g. of sulfur tetrafluoride to the pressure vessel by a length of copper tubing having a $\frac{1}{16}$ -in. bore and $\frac{1}{8}$ -in. outside diameter (Note 3).

The pressure vessel is heated with agitation at 100° for 4 hours and at 130° for 6 hours. The vessel is allowed to cool to room temperature and the volatile by-products [*Caution! Toxic!* (Note 4)] are vented. The crude, fuming, liquid product (Note 5) is poured into a stirred suspension of 10 g. of finely divided sodium fluoride in 60 ml. of pentane (Note 6), the mixture is filtered, and the filtrate is fractionated through a 6-in. Vigreux column. 1,1,1-Trifluoroheptane is collected at 100–101°/760 mm., n_D^{25} 1.3449. The yield is 21.7–24.6 g. (70–80%).

2. Notes

1. The pressure vessel should be lined with Hastelloy-C, stainless steel, or other metal resistant to attack by hydrogen fluoride, because the latter substance is a by-product of the reaction. The pressure vessel employed should be safe for use at 500 atm. pressure and should be equipped with a rupture disk rated at 500 atm. If the equipment available is rated for use only at lower pressure, the size of the charge should be reduced appropriately.

2. Sulfur tetrafluoride is obtainable in one-pound cylinders from the Organic Chemicals Department of E. I. du Pont de Nemours and Co., Wilmington, Delaware. Directions for its synthesis by the action of sodium fluoride on sulfur dichloride in acetonitrile have been published,² and a more detailed version of these directions has been submitted to *Inorganic Syntheses*.

3. It is also possible to connect the supply cylinder of sulfur tetrafluoride to the pressure vessel by a short length of butyl rubber vacuum tubing.

If the supply cylinder of sulfur tetrafluoride contains more than 65 g., it may be placed on a balance in order to determine when the required amount has been transferred to the pressure vessel.

4. Since the volatile gases include sulfur tetrafluoride and thionyl fluoride, which possess toxicities comparable to that of phosgene, caution must be exercised in their disposal. A suitable procedure is to condense the volatile gases in a trap cooled in a mixture of acetone and solid carbon dioxide, and then to allow this material to pass slowly through an empty polyethylene bottle, which serves as a safety trap, and into a stirred aqueous potassium hydroxide solution.

5. If it is found necessary to retain the crude product for any period of time before working it up, it may be conveniently stored in a polyethylene bottle or other container resistant to attack by hydrogen fluoride.

6. As indicated above, the crude product contains hydrogen fluoride. The sodium fluoride disposes of this by-product by the reaction $\text{NaF} + \text{HF} \rightarrow \text{NaHF}_2$. An alternative procedure is to pour the crude product into water and to separate the product by extraction with pentane.

3. Methods of Preparation

1,1,1-Trifluoroheptane has been prepared only by the action of sulfur tetrafluoride on heptanoic acid.³

4. Merits of Preparation

The described procedure is useful for the preparation of a wide variety of compounds containing trifluoromethyl groups from the corresponding carboxylic acids.³ The yields are generally 60–90%. Some representative examples are listed in Table I. In the cases of the difunctional acids, only 0.1 mole of the compound should be used in the procedure.

TABLE I

Product	B.P., °C.	n_D^{25}
1,1,1-Trifluorododecane	92 (12 mm.)	1.3896
1,1,1-Trifluorohexadecane	107 (0.3 mm.)	1.4148
1,1,1-Trifluoro-3,5,5-trimethylhexane	121–122	1.3657
(4,4,4-Trifluorobutyl)cyclohexane	172–173	1.3987
1,1,1,10,10,10-Hexafluorodecane	183–184	1.3519
1,1,1,6,6,6-Hexafluoro-3-hexene	90–91	1.3131
<i>p</i> -Bis(trifluoromethyl)benzene	113–115	1.3767
2,4-Bis(trifluoromethyl)chlorobenzene	147	1.4130
<i>p</i> -Trifluoromethylnitrobenzene	(m.p. 41–43°)	

Carboxylic anhydrides and esters react with sulfur tetrafluoride to give the same products as the acids only at elevated temperatures, i.e., 200° to 300°.

¹ Contribution No. 572 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Co., Wilmington, Del.

² C. W. Tullock, F. S. Fawcett, W. C. Smith, and D. D. Coffman, *J. Am. Chem. Soc.*, **82**, 539 (1960).

³ W. R. Hasek, W. C. Smith, and V. A. Engelhardt, *J. Am. Chem. Soc.*, **82**, 543 (1960); W. C. Smith, U. S. pat. 2,859,245 (1958).

SUBJECT INDEX

(This index comprises material from Volumes 40 and 41 only; for previous volumes see Collective Volumes 1, 2, and 3 and Volume 39.)

Names in small capital letters refer to the titles of individual preparations. A number in ordinary boldface type denotes the volume. A page number in boldface italics indicates that the detailed preparative directions are given or referred to; entries so treated include principal products and major by-products, special reagents or intermediates (which may or may not be isolated), compounds mentioned in the text or Notes as having been prepared by the method given, and apparatus described in detail or illustrated by a figure. Page numbers in ordinary type indicate pages on which a compound or subject is mentioned in connection with other preparations.

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